Diabetes and Metabolic Syndrome in Middle-aged and Elderly Adults: a Population-based Study in Jiangsu Province, China

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ABBREVIATIONS

Apo A	Apolipoproteins A
Apo B	Apolipoproteins B
ATP III	the National Cholesterol Education Program Adult Treatment Panel III
BMI	Body mass index
CRP	C-reactive protein
CVD	Cardiovascular diseases
DBP	Diastolic blood pressure
FDP	Fibrin degradation products
FFA	Free fatty acid
FPG	Fasting plasma glucose
HDL-C	High-density lipoprotein cholesterol
HOMA-IR	Homeostasis model assessment of insulin resistance
IDF	International Diabetes Federation
IFG	Impaired fasting glucose
IL-6	Interleukin-6
LDL-C	Low-density lipoprotein cholesterol
MetS	Metabolic syndrome
OGTT	Oral glucose tolerance test
PAI-1	Plaminogen activator inhibitor-1
SBP	Systolic blood pressure
TC	Total cholesterol
TG	Triglycerides
TNF-α	Tumor necrosis factor-α
TPA	Tissue plasminogen activator
VWF	Von Willebrand factor
WC	Waist circumference
WHO	World Health Organization
WHR	Waist-to-hip ratio

ABSTRACT

Diabetes and Metabolic Syndrome in Middle-aged and Elderly Adults: a Population-based Study in Jiangsu Province, China

A cooperative project between

Faculty of Medicine, University of Oslo, Norway

Jiangsu Provincial Centers for Disease Prevention and Control, China

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BACKGROUND: Chronic diseases like diabetes and metabolic syndrome are increasing rapidly in China. The present study was a part of an ongoing prospective follow-up project aiming to develop necessary health strategy.

OBJECTIVE: The aim of this study was to evaluate the prevalence of diabetes and metabolic syndrome and to identify their associated risk factors among middle-aged and elderly participants in Jiangsu province, China.

RESEARCH DESIGN AND METHODS: As the baseline survey of a follow-up programme, this population-based cross-sectional study was performed on 3914 adults aged 35-74 years living in urban and rural areas of 4 cities in Jiangsu province, eastern China. The prevalence of diabetes and metabolic syndrome was assessed according to WHO, IDF and modified ATP III criteria. Potential socio-demographic and lifestyle risk factors were also analyzed. Data was collected by interviewer-administered questionnaire, biophysical assessment and biochemical examination.

RESULTS: Age-Standardized prevalence of diabetes and IFG was 6.8% and 21.0% respectively. Family history of diabetes was an important predictor of diabetes in the study population. However, BMI was found as the strongest significant risk factor for the development of diabetes. The adjusted prevalence of metabolic syndrome defined by WHO, IDF and modified ATP III criteria was 12.3%, 21.8% and 31.5%, respectively. Gender, age and BMI status were significant risk factors for metabolic syndrome independent of definition, while higher education level for WHO MetS, habit of tea consumption for modified ATP III MetS were protective factors in the study population. The diabetes and metabolic syndrome were more common in female than in male ($p<0.05$). Substantial agreement ($\kappa=0.79$) was found between IDF and modified ATP III definitions. In addition, weight gain was particularly risk factor for each disorder among originally normal weight population ($p<0.001$).

CONCLUSIONS: Diabetes and metabolic syndrome were highly prevalent in middle-aged and elderly Chinese population. Community-based strategies for lifestyle modification are of great necessity to address the problems.

1. INTRODUCTION

1.1 Worldwide burden of chronic noncommunicable diseases

When infectious disease is still threatening people's health, chronic diseases, including cardiovascular diseases (CVD), diabetes, obesity, cancer and chronic respiratory diseases, are nowadays the major cause of death and disability worldwide(1). The report from World Health Organization showed that, approximately 35 out of the 58 million deaths were related to chronic disease in 2005 (1). Furthermore, these diseases increasingly affect people, families and communities globally due to increasing degree of underlying determinants for the diseases like globalization, urbanization and population ageing, and so on. For example, overweight and obesity in child and adolescent are increasing worldwide(2, 3). The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030(4).

In developed countries like the United States, chronic diseases account for 70% of all deaths in the country, which is 1.7 million each year(5). Whereas, more than 80% of these diseases occurred in low- and middle-income countries(6). In 2006, the estimated losses as a result of coronary heart disease, stroke, and diabetes ranged from $20–30 million in Ethiopia and Vietnam, and near $1 billion in populous countries such as China and India(6).

However, another important fact is that a relatively few and preventable risk factors cause the majority of the chronic disease burden(1). Unhealthy diet, physical inactivity, tobacco use are the most common modifiable risk factors. It is almost the same in men and women, similar in every part of the world. In conjunction with non-modifiable risk factors (age and heredity), they can explain the majority of new events of chronic diseases.

Although chronic diseases are very common, they are invisible. So far, whether the global goal for chronic disease prevention and control set by WHO(6) can be achieved in the future remains unknown(7). But, convincing evidence indicates that adopting healthy

behaviors such as eating nutritious foods, being physically active and avoiding tobacco use can largely prevent or control the adverse effects of these diseases.

1.2 Diabetes mellitus

1.2.1 Diagnosis and classification of diabetes mellitus

The recommendations for the classification, diagnosis, and screening of diabetes are revised every few years, reflecting updated knowledge from research and clinical practice(8). For example, in 1997, the American Diabetes Association (ADA) recommended that the cut-off point for fasting plasma glucose (FPG) for diabetes should be reduced from 7.8 to 7.0 mmol/l, and arabic numerals should be used for type of diabetes instead of roman numerals(9). In 2003, follow-up report from ADA suggested the cut point for IFG should be further reduced from 6.1 to 5.6 mmol/l(10).

Based on the latest recommendations from American Diabetes Association (ADA) in Jan. 2008(11), classification of diabetes mellitus are as follows:

I. Type 1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency)
II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance). It accounts for about 90-95% of those with diabetes.
III. Other specific types (genetic defects of β-cell function, genetic defects in insulin action, endocrinopathies, and so on)
IV. Gestational diabetes mellitus (GDM)

Diagnosis criteria for the diabetes are:

Fasting plasma glucose≥126 mg/dl (7.0 mmol/l).

OR

Symptoms of hyperglycemia (including polyuria, polydipsia, and unexplained weight loss) and a casual plasma glucose≥200 mg/dl (11.1 mmol/l).

OR

2-h plasma glucose≥200 mg/dl (11.1 mmol/l) during an OGTT, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

These criteria to diagnose diabetes should be confirmed by repeat testing on a subsequent day, in the absence of unequivocal hyperglycemia.

1.2.2 Prevalence and trends of diabetes globally

Diabetes is one of the most costly and burdensome chronic diseases of our time and is increasing at an alarming rate becoming one of the major public health problems throughout the world(12). The adverse effects on health root in the broad spectrum of acute and chronic complications of the disease. Diabetes, particularly Type 2 diabetes, has risen steadily during recent decades and continues to increase in the future. According to the findings from American Diabetes Association (ADA) in 2004(4), the prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030, which is shown in Figure 1.1(4).

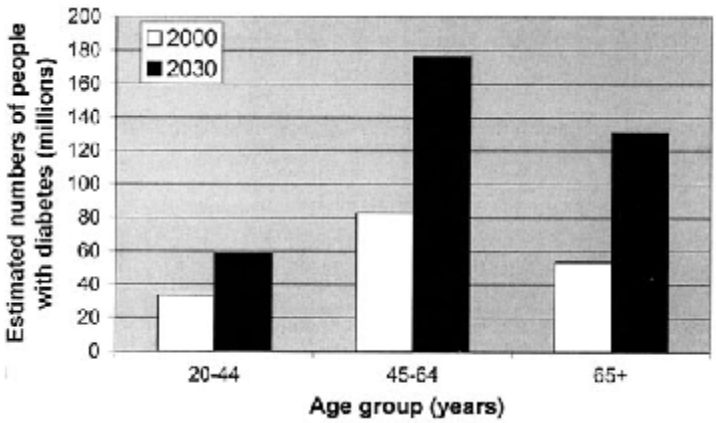


Figure 1.1 Estimated numbers of adults with diabetes by age group, year in the world.

Just taking one specific country as a example, the prevalence of diabetes, impaired fasting glucose, and insulin resistance was high and their prevalence continues to increase in the United States from two nationally representative samples of the adult population during the periods 1988-1994 and 1999-2002(13).

The prevalence of diabetes is also substantial in adolescents. For example, a cross-sectional study in USA(14), using data from National Health and Nutrition Examination Survey (1999-2002), found that 0.5% of adolescents reported having diabetes. Of those reporting diabetes, 71% were type 1 and 29% as having type 2 diabetes. And, 11% of them had impaired fasting glucose levels. In children, an earlier onset of Type 1 diabetes has been observed, and also the incidence of Type 2 diabetes among young people is increasing(15).

However, the prevalence of diabetes varies in different countries and different ethnic groups. Additionally, it is higher in developed countries, but the largest relative increase will occur and the greatest impact will be given in the developing countries(8, 16). The main reasons are both aging of the population and increasing urbanization(16).

1.2.3 Diabetes in China

Diabetes has become an important public health challenges in developing countries. China is the second top country with highest numbers of people with diabetes in the world only after India mainly due to both aging of the population and dramatic urbanization(4).

During past few decades, several large-scale observational surveys have robustly figured out the estimation of diabetes in mainland China. The prevalence of Type 2 diabetes and impaired glucose tolerance was reported to be about 1%, respectively among a sample of 110,660 men and women aged 25 to 74 years living in Daqing City, northeast China in 1986(17). More representative study, the 1994 China National Diabetes Survey examination of 213,515 subjects aged 25 to 64 years yielded prevalence estimates for diabetes and impaired glucose tolerance of 2.5% and 3.2%, respectively. And the prevalence of diabetes was three times higher then it was 10 years ago(18). More recently, InterASIA study conducted in 2000-2001 including nationally representative sample of 15,540 adults aged 35-74 years, reported that the prevalence of self-reported diagnosed

diabetes, undiagnosed diabetes, and impaired fasting glucose were 1.3%, 4.2%, and 7.3%, respectively. The age-standardized prevalence of diabetes was higher in the north and in urban areas(19). Obviously, the rate increased and it is foreseeable to continue along with the time if no intervention in despite of diagnostic criteria were slightly different in different studies.

In elderly, reliable results from the 2002 National Nutrition and Health Survey in China indicated that adjusted prevalence of diabetes in 9925 subjects aged ≥60 years was 6.8%. It was higher in female and in the city(20).

In children and adolescences, figure also from the 2002 National Nutrition and Health Survey in China reported that, the overall prevalence of diabetes in subjects aged 5-17 years was 0.19%. It was higher in urban areas compared to rural counterparts(21). But based on another cross-sectional screening program in Beijing area in 2004, the prevalence rates of diabetes and IFG among 19,593 schoolchildren were 0.6% and 1.4%, respectively(22), which were much higher than national average level two years before.

1.3 Metabolic syndrome

In the last number of years, a great deal of concern has been given to a cluster of metabolic abnormalities including abdominal obesity, hyperglycemia, hypertension and adipose metabolic disorder identified as metabolic syndrome (MetS). It is regarded as the independent risk factor of cardiovascular disease (CVD) and Type 2 diabetes mellitus (T2DM)(23-25). These chronic diseases are all characterized with long term, bad prognosis and tremendous social and financial burdens. MetS and diabetes are even more serious than HIV/AIDS in morbidity and mortality(26). However, there were some debates on the use of the term “metabolic syndrome”(27, 28) because it lacks a perfect explanation at pathophysiological level although certain CVD risk factors are prone to cluster. So far, it is still premature to introduce the current definitions of MetS into clinical practice. Single risk factors can be treated appropriately and improved by the non-pharmacologic approaches(29).

1.3.1 Definitions of metabolic syndrome

Several organizations have issued definitions in an attempt to heighten awareness and identify patients who ultimately may be at increased risk for CVD(8). The name of MS changed for several times since the first work of Reaven in 1988(30), so did the diagnostic criteria. Up to now, dispute on the different definitions of MS never cease. Nevertheless, the most frequently used criteria were proposed by World Health Organization (WHO)(31), International Diabetes Federation (IDF)(32), and the National Cholesterol Education Program Adult Treatment Panel III (ATP III)(33) respectively. These definitions share several core features: obesity, insulin resistance, dyslipidaemia and hypertension. However, they also include important differences. WHO regards insulin resistance as the major underlying pathophysiological abnormality, while ATP III and IDF definitions identify abdominal obesity measured as increased waist circumference as the key driver of the syndrome. Detailed measurements and categorical cutoff points for these three definitions were shown in Table 1.1.

Table 1.1 Diagnostic criteria for MetS from WHO, IDF and ATP III(2005)

	Measure	Categorical cutpoints
WHO (1999)	**The presence of glucose intolerance, IGT or T2DM and/or IR, together with two or more of the following components:**	
	Central obesity	WHR>0.9(male), >0.85(female) and/or BMI>30 kg/m^2
	Dyslipidaemia	TG≥1.7 mmol/l and/or HDLC≤0.9 mmol/l in men, HDLC≤1.0 mmol/l in women
	Blood pressure	≥140/90 mmHg
	Glucose	IGT, IFG, or T2DM
	microalbuminuria	Urinary albumin excretion ratio≥20 μg/min or albumin:creatinine ratio≥30mg/g
IDF (2005)	**Central obesity (Waist circumference ethnically specific) + any 2 of 4 other criteria:**	Waist circumference≥90cm (male), ≥80cm (female) for Chinese
	Raised TG	≥150mg/dl (1.7 mmol/l) or on specific treatment for this lipid

		disorder
	Reduced HDLC	<40 mg/dl(1.03 mmol/l, men), <50 mg/dl (1.29 mmol/l, women) or on specific treatment for this lipid abnormality
	Raised blood pressure	SBP≥130 mmHg or DBP≥85 mmHg or on treatment for previously diagnosed hypertension
	Raised fasting glucose	Fasting plasma glucose≥100mg/dl (5.6 mmol/l) or previously diagnosed Type 2 diabetes
ATP III (updated by AHA/NHLBI, 2005)	**The presence of 3 or more of these components:**	
	Elevated waist circumference	≥90cm(men), ≥80cm(women)
	Elevated TG	≥150mg/L (1.7 mmol/l)
	Reduced HDLC	<40 mg/dl(1.03 mmol/l, men), <50 mg/dl (1.29 mmol/l, women)
	Elevated blood pressure	≥130/85 mmHg
	Elevated fasting glucose	≥100mg/dl (5.6 mmol/l)

1.3.2 Prevalence and trends of metabolic syndrome globally

Globally, the prevalence of metabolic syndrome is high and this prevalence is steadily increasing worldwide. Because it is considered as one of important drivers of cardiovascular disease (CVD) and Type 2 diabetes as addressed above, the public health impact of the syndrome is considerable. Its prevalence varies in various populations due to different sociodemographic characteristics and different MetS definitions(34).

In the United States, by using the data from the Third National Health and Nutrition Examination Survey and ATP III definition, Earl S. Ford et al. reported that the age-adjusted prevalence of MetS among US adults was 23.7%, with highest affects in Mexican Americans(35). Also using this representative national survey data, Ferranti et al. estimated nearly 1 in 10 children aged≥12 years had MetS, and it had a similar racial/ethnic distribution with adults(36).

When moving to the Europe, the overall prevalence of the metabolic syndrome in non-diabetic adults was 15%, by using modified World Health Organization definition of MetS. The age-standardized prevalence of MetS was slightly higher in men (15.7%) than

in women (14.2%)(37).

In Asia, the overall age-adjusted prevalence of metabolic syndrome was 24.6% (NCEP ATP III criteria) in the combined urban and rural population sample in India(38), and 24.9% in urban population(39). By using Korean National Health Examination and Nutrition Survey (KNHENES) data in 1998 and 2001, the prevalence of metabolic syndrome among Korean adults was found to be 15-30% according to various criteria of metabolic syndrome. Moreover, the rate increased significantly from the year of 1998 to 2001(40). From information of the Japanese National Health and Nutrition Survey (NHNS) in 2003, and according to the Japanese diagnostic criteria, the overall prevalence of MetS was discovered to be 22.8% for males and 8.7% for females(41). Moreover, the prevalence of MetS was found to vary from <3% in rural Bangladeshi women(42), 15% in Thailand(43), and 33.7% in Iran(44). Particular information of metabolic syndrome in China was discussed in the next section.

1.3.3 Metabolic syndrome in China

Like other countries undergoing rapid urbanization and nutrition transition in the world, westernized lifestyle characterized by a combination of excessive energy intake and inadequate physical activity is becoming more and more prevalent in China during few decades of years. As a result, metabolic syndrome has been one of important public health problems. And also, this condition has impact not only on adults, but also on children and adolescents, having more effect in urban area than in rural areas in despite of different degree. This can be demonstrated from several available studies conducted in China.

For example, study conducted in 11 provinces in 1992 indicated that the prevalence rate of metabolic syndrome was high (13.3%, 12.7% in males, 14.2% in females), and it increased with age(45). From another study conducted in eastern China in 2002, the prevalence of the syndrome among adults without diabetes was 34.3% for men, 24.1 for women in urban areas, 2.7% for men and 11.4% for women in rural areas, when using

modified ATP III definition(46). Based on survey in one district in Beijing City in 2005, the standardized prevalence of MetS was found to be 13.4%, which was slightly lower than overall rate in Beijing and Shanghai(47). But in Jiangsu province, the prevalence was reported as 15.9% (standardized) in adults aged above 20 years in 2006(48).

In rural area, the age-adjusted prevalence of MetS for adults 25 to 64 years old was 3.2%, 4.9%, and 3.9% in men and 7.2%, 11.5%, and 10.9% in women, respectively in the sample of 18,630 adults 25 to 64 years old from Anhui Province, according to ATP III, modified ATP III and IDF criteria(49).

In children and adolescents, MetS was still relatively low in general, but MetS prevalence among Chinese overweight adolescents was similar to those living in the USA. This was the estimation from national representative sample in the 2002 China National Nutrition and Health Survey. Li et al. reported that the overall prevalence of the metabolic syndrome in 2761 adolescents aged 15-19 years was 3.7% by applying the criteria for US adolescents. Urban boys had the highest rate (5.8%) compared with girls and rural youngsters(50). In addition, a school-based survey in Beijing in 2006 found that the overall prevalence of MetS among adolescents aged 14–16 years was 3.3%, and it increased significantly with BMI(51). But, the MetS has reached a high level in some areas today. For example, MetS has already affected 10.3% obese children and adolescents in Zhejiang Province, southeast of China(52).

1.4 Associated factors for diabetes and metabolic syndrome

Although the precise etiology of most cases of diabetes and MetS remains uncertain, Contributing factors have been well established and well known(1). Some like lifestyle factors have been further confirmed by a great deal of intervention researches. It is considered that underlying determinants like urbanization, population aging lead to appearance of a set of risk factors described below. And those risk factors cause the disease by the intermediate of raised blood pressure, elevated glucose level, abnormal blood lipids, and so on. The relationship between the major modifiable risk factors and

the diseases is similar in all regions of the world.

There are three points which need to be mentioned here. One is that diabetes and metabolic syndrome, complex metabolic diseases, share almost all of common risk factors. And also, metabolic syndrome itself is thought to a major risk factor for Type 2 diabetes. The second, the degree and distributions of these risk factors are diverse in different area and populations. The third, these risk factors, which include genetic, environmental, and lifestyle ones, interact with each other, possibly having synergy on the occurrence of diseases, although some of them are independent determinants.

Compelling evidence from metabolic studies, large prospective observational studies, and clinical trials indicate that unhealthy diet, overweight/obesity, and sedentary lifestyle are major contributors to the diabetes epidemic(8). So do the metabolic syndrome. In addition, there are also other modifiable risk factors including smoking, alcohol drinking, inflammation, etc(53, 54). These are the target of intervention approaches.

1.4.1 Socio-demographic factors

These factors include age, gender, ethnicity, family history of diabetes, etc. Of course, they belong to non-modifiable factors but still worth mentioning solely.

The risk of diabetes, metabolic syndrome and its components increases markedly with age. Even with identical BMI, the elderly is much more likely to develop the disease than the youth. And in recent decades, the age of onset has moved down into younger adults and even adolescents(54). Sex and racial differences were often observed in many studies on diabetes and MetS, regarding the rate of disease, the distribution of risk factors, etc.

People who have family members with diagnose of Type 2 diabetes are at a greater risk for developing it themselves. Nevertheless, having a genetic disposition towards diabetes is not a guarantee of developing diabetes. Modifiable factors play an important role in determining the final result on the basis of giving genetic background.

1.4.2 Overweight and obesity

Finding from epidemiological studies have repeated confirmed a strong positive association between excess adiposity and risk of developing Type 2 diabetes(8). The increasing prevalence of obesity was the single most important risk factor and largely responsible for the increase in the prevalence of Type 2 diabetes(16, 55). Greater weight means a higher risk of insulin resistance, because fat interferes with the body's ability to use insulin. Furthermore, interventions aiming at reducing obesity also reduce the incidence of Type 2 diabetes and metabolic syndrome. Body mass index (BMI) is the most commonly used parameter for overweight and obesity. However, several studies indicated that waist circumference or waist-to-hip ratio, which reflects visceral (abdominal) fat, may be better indicators of the risk of developing Type 2 diabetes than body mass index(54).

The prevalence of overweight and obesity is increasing dramatically in adults in the world. But more important, the increasing prevalence of obesity in children and adolescents is a particular concern(16).

Other than excess adiposity, weight gain is also an important predictor of developing Type 2 diabetes and metabolic syndrome. Just one example, based on data from a large prospective cohort, Oguma et al. found that, weight gain significantly increased the risk of Type 2 diabetes, and that a low initial BMI does not ameliorate the increase in risk of type 2 diabetes with weight gain(56).

1.4.3 Dietary factors

Diet is one crucial aspect of lifestyle. Messages from a large number of epidemiological studies indicate that unhealthy diet including a high total calorie, low dietary fiber intake, a high glycaemic load, a low polyunsaturated to saturated fat ratio, etc. is thought to contribute to the development of chronic diseases including diabetes and metabolic syndrome. Studies found that, high fiber content, n-3 fatty acids, and antioxidants, as well as phytochemicals from olive oil, legumes, whole grains, fruits, and vegetables, might be

responsible for its beneficial effect on the prevention and control of diabetes and metabolic syndrome.

Besides, unhealthy diet can lead to MetS components like overweight/obesity, high blood pressure, dyslipidemia, indirectly and thereby lead to the occurrence of metabolic syndrome.

Convincing evidence from the prospective studies consistently showed a reduced risk for high intake of whole grain foods or cereal fiber on the development of Type 2 diabetes (57). Actually, diet together with other lifestyle modification is the basis in the prevention and management of Type 2 diabetes. A study(58) even documented that adjustment of diet composition without weight loss or pharmacologic intervention could improve the hyperglycemia of Type 2 diabetes.

1.4.4 Physical activity and sedentary lifestyle

Physical inactivity has been found, in both cross-sectional and longitudinal studies, to be an independent predictor of Type 2 diabetes in men and women(54). It is also a major contributor to the global increase of obesity. Both low sedentary and high exercise activities contribute to increased energy expenditure, improved weight control and prevention of obesity(59). Increased physical activity can prevent the weight gain associated with aging at least two times greater in individuals who were more active compared with those who were inactive(60). Evidence from epidemiological studies indicates that physically active persons have a lower incidence of diabetes and metabolic syndrome. Physical activity can reduce 35% of the risk for diabetes, which was found from a literature review(60). It can also reduce the risk of Type 2 diabetes in people with prediabetes (IGT and/or IFG) independent of diet or weight loss.

Other than the prevention, exercise has been recommended a treatment for Type 2 diabetes, metabolic syndrome, and some other chronic diseases. Moreover, the effectiveness of physical exercise depends on the type frequency, the intensity and the

duration of it.

1.4.5 Inflammation

In recent years, it has been demonstrated that chronic, low-level tissue inflammation related to obesity contributes to insulin resistance, the major cause of Type 2 diabetes. And also, Chronic subclinical inflammation is associated with metabolic syndrome, as indicated by an increase in circulating levels of proinflammatory cytokines, which was supported by Insulin Resistance Atherosclerosis Study (IRAS) and follow-up(61). So far, inflammatory markers discussed in the researches include C-reactive protein (CRP), TNF-α, plasminogen activator inhibitor (PAI)-1, fibrinogen, and so forth.

For example, C-reactive protein (CRP) was regarded as a sensitive marker of systemic low-grade inflammation and was an important predictor of type 2 diabetes(62).

1.4.6 Other non-modifiable factors

In this sort, they comprise history of gestational diabetes, polycystic ovary syndrome in female, birth weight, and so on.

Gestational diabetes affects about 4% of all pregnant women. It begins when hormones from the placenta make the mother insulin resistant. Women who had gestational diabetes have substantially higher risk of developing Type 2 diabetes in later life. Their babies are also at some risk for developing diabetes in later life.

Another example, a meta-analysis(63) including 14 studies (132,180 persons) indicated that U-shaped, not linear relationship existed between birth weight and diabetes risk in later life, which meant low birth weight and high birth weight were associated with increased risk of diabetes to the same degree.

1.5 Follow-up study on metabolic syndrome and diabetes

Follow-up study discussed here means observational cohort study, which observes the outcomes of exposure over a period or at intervals in persons exposed to risk, without any intervention measurements. Because exposure information is collected before outcomes, it is more reliable and more powerful for testing casual hypothesis than cross-sectional study. Therefore, it is worth conducting if conditions permit.

During the past few years, several different definitions for MetS have been issued with the main purpose to identify individuals at high risk for cardiovascular diseases. Prospective follow-up studies regarding metabolic syndrome as exposure have been performed in USA, Finland, Italy, and so on (64-66). They, but not all, shown that MetS was related to increased risk of cadio-cerebrovascular diseases such as stroke(65), coronary heart disease, cardiovascular events(66), cardiovascular mortality(67), heart attack and mortality(64) and so forth. MetS in childhood was also associated with adult cardiovascular disease in the future(68).Moreover, researchers also found that MetS predisposed to depressive symptoms(69), impaired cognitive function(70).

Evaluation on the predictive ability of different MetS definitions can also be performed in follow-up study, as they did in USA(71) and in Italy(72).

As demonstrated above, not all studies consistently drew the same conclusions. For example, it was reported that MetS was a significant predictor of CVD and Type 2 diabetes, especially the latter in England(73). And also, Wang et al. reported MetS can predict incident diabetes in Beijing Chinese population(74). But, in another study, Cameron et al. called for a debate by drawing an opposite conclusion that a single fasting glucose measurement was more effective and efficient than MetS by published definitions in predicting incident diabetes in giving adult population(75).

Unlike metabolic syndrome, follow-up study which looked on diabetes as exposure has been relatively scarce possibly because diabetes itself is a serious disease normally as endpoint. Nevertheless, some studies evaluated diabetes as predictor of other diseases or mortality. The researchers found that diabetes increased the risk of endometrial cancer in

Norwegian women during 15.7 years of follow-up(76), diabetes had a strong synergistic effect together with depression on excess mortality(77). There were also some studies which evaluated health management of diabetic patients or complications occurrence. For instance, many children and adolescents with T2DM were found insufficient adherence to diabetes centers in general practice and lifestyle intervention as sole treatment was not often useful for long-term metabolic control(78).

1.6 Intervention epidemiology

Leaving high risk groups or patients alone after awareness is unacceptable, and prevention is the best management for them. It is particularly important to effectively implement and strengthen population-based primary prevention strategies since it is the most cost-effective form of health care(79). The prevention of diabetes by the change of the lifestyle or if necessary some drugs become a major concern worldwide(57, 80, 81). Actually, several intervention studies, including lifestyle modification and drug treatment, have been done and consistently demonstrated the progression to Type 2 diabetes can be prevented or deferred in those persons at high risk from diverse racial backgrounds and across all age groups.

The intervention studies were performed both in developing countries like China(82), India(81) and in developed countries like Sweden(83), Finland(80, 84, 85), the United States(86).

Most interventions on diabetes had a couple of similar characteristics: (a) Intervention measurement mainly included dietary change (less fat intake, more vegetable consumption, more fiber intake, etc.), or exercise training, or a combination of both. (b) Target population was individuals with impaired glucose tolerance (IGT), a particularly high risk group. (c) If drug was used as a way of prevention of diabetes in the interventions, generally it was metformin. (d) The conclusions were consistent, i.e. these intervention measurements could reduce the incidence of diabetes in local population at different degree. But, detailed approaches used to implement the intervention were

different from study to study.

For example, Indian Diabetes Prevention Programme (IDPP) has demonstrated that moderate but consistent lifestyle modification or therapeutic intervention with metformin could prevent or delay progression of IGT to diabetes with relative risk reductions of 28.5 and 26.4%, respectively(81), and these kind of intervention were cost-effective(87). Furthermore, the most recently intervention on diabetes was found as DE-PLAN project in Europe(88), which involved 17 European countries so far, and it is still on the process.

To sum up, intensive diet and lifestyle modification can largely reduce the risk of Type 2 diabetes which is more effective than drugs although both had encouraging effects. In addition, diet and lifestyle modification are considered the cornerstone in the prevention and management of Type 2 diabetes(8).

Because of sharing some common risk factors, intervention on metabolic syndrome was similar with the diabetes prevention. Lifestyle changes (diet and physical activity) were regarded as the first-line approaches and these approaches were proven to be effective (89-91). Since MetS is a combination of cardiovascular disease risk factors, its intervention or treatment actually was aiming at reverse of single metabolic abnormities. So, very few studies have been conducted especially targeting at MetS up to now. Effect of intervention on MetS and its components were also analyzed in diabetes prevention study(89, 92).

But, one important issue that is worth of note is post-study sustainability of intervention. Although most of these studies were found effective in achieving short term effect, very limited evidence can be found regarding long-term effect of intervention and maintenance of lifestyle correction.

2. RATIONALE AND OBJECTIVES

2.1 Rationale

As stated above, metabolic syndrome and diabetes have reached epidemic proportion and are increasing rapidly especially in countries with economic transition like China in which dramatic urbanization and nutrition transition are occurring(93). Actually, chronic diseases such as metabolic syndrome, diabetes have been identified as significant public health problems in China since early 1990s. A MetS study which was conducted in 11 provinces in 1992 indicated that the prevalence rate of metabolic syndrome was high (13.3% total, 12.7% in males, 14.2% in females, mean age 50.6 years old), and it increased with age(45).

In eastern China, Jiangsu province is relatively developed area with more health challenges associated with socioeconomic development. According to the 2002 National Nutrition and Health Survey in China, the prevalence of the MetS components in adults in Jiangsu province was quite high. Standardized prevalence rates of hypertension, diabetes and dyslipidemia in representative subjects aged ≥18 years were 19.3%, 2.6% and 17.8%, which were much higher in elderly groups. The prevalence rate of overweight/obesity was 29.0% in general(94). Due to constant increase of aging people, developing economics and consequential changes in lifestyle and diet, etc, it is fully reasonable to assume that the hazard of MetS is becoming more serious than before. In order to develop sound health policy to cope with the challenges related to lifestyle change, we need to identify the extent of the problem and its risk indicators.

However, very limited data is available for the prevalence of MetS and diabetes in large scale, population-based study in China. Even within Jiangsu province, little is known and no updated information is available about the epidemiology of MetS and diabetes.

2.2 Objectives

Overall objective was

To evaluate the prevalence of diabetes and metabolic syndrome among middle-aged and elderly participants in Jiangsu province, China. Furthermore, its associated risk factors were also analyzed.

Specific aims were

1. To estimate the prevalence of diabetes, IFG and hyperglycemia in Chinese adults.
2. To determine the association between selected socio-demographic, behavioral variables and diabetes in Jiangsu, China.
3. To describe the sex- and age-specific prevalence and distribution of metabolic syndrome among adults aged 35-74 years in Jiangsu province, China.
4. To identify the determinants for metabolic syndrome using WHO, IDF and ATP III definition, respectively.
5. To assess the agreement between different definitions of metabolic syndrome.
6. To investigate the correlation between FPG and other variables including inflammation biomarkers in selected subsample.

3. MATERIALS AND METHODS

It was population-based cross-sectional study focused on the prevalence, main risk factors and their degrees of MetS and diabetes in Jiangsu province. Data was collected through questionnaire interviews, body examination on anthropometry variables and blood analysis. Anthropometric test and blood sampling were conducted at the time of interview.

3.1 Brief description of the study area

3.1.1 Geography and climate

Jiangsu, an eastern province in mainland China, covers an area of 0.1 million square kilometers (1.06% of the total area of the country). There are two great rivers flowing through the whole province: Yangtze River from west to east and Beijing-Hangzhou Grand Canal from north to south. With Yellow Sea to its east, Jiangsu adjoins Anhui and Shandong provinces in the west and north respectively, with Zhejiang province and Shanghai Municipality as its neighbors in the southeast (Figure 3.1). Located in the prosperous Yangtze Delta, Jiangsu has a large area of plain as its typical topography, and

dotted with two of the top five freshwater lakes in China. Jiangsu thus enjoys the superiority of its natural condition and lays a solid economic foundation.

Figure 3.1 Geographical location of Jiangsu province in China

Situated in a transition belt from a subtropical to temperate zone, the province has a typical monsoon climate(95). Generally, it is mild with moderate rainfall and clear distinction of the four seasons.

3.1.2 Socio-demographic characteristics

Jiangsu consists of 13 prefectures which include 54 city districts and 52 counties. The total population in the province is 75.5 million, with balanced gender ratio(95). It is populated by Han (99.67%), Hui, Man and other ethnic groups.

Jiangsu is one of the most densely populated provinces in China. And also it is one of the most economically developed areas in China, with 10.3% of national GDP only after Guangdong Province.

Infant mortality rate is 5.95‰ and mortality rate of children under 5-year is 7.62‰(95). Average life expectancy in Jiangsu is 74.13 years. The proportion of the population ≥60 years in 2000 was 8.8%, and it is projected to be 20.5%, 29.0% in 2020 and 2040, respectively. It is characterized by female elderly dominating the proportion, higher

growth rate of the elderly than that of economic development and unbalanced distribution(96).

3.1.3 Urbanization and nutrition transition

At present, more than half of the population lives in the cities and towns. And also, Jiangsu is one of the provinces in China with highest speed of urbanization. Urbanization level increased from 20% to 50% only within 15 years (97).

Rapid urbanization has important impact on nutrition. The long-term trend of nutrition is a shift from traditional Chinese diet towards a diet with high fat, high energy density and low dietary fiber(98). These changes resulted in rapid increases the prevalence of overweight/obesity and dietary-related chronic non-communicable diseases in urban residents.

3.1.4 Health challenges in adults in Jiangsu province

Infectious disease decrease rapidly in Jiangsu. In contrast to that, owing to continuous aging of population, urbanization, unhealthy lifestyle, etc., chronic noncommunicable disease, including cardiovascular diseases (CVD), diabetes, cancer, etc. has been the most serious public health problems in the province. It is responsible for about 70% of deaths in the province(99). It is estimated that about 7 million hypertension patients, 2.2 million people with diabetes, 0.6 million people with coronary heart disease in the whole province at present(99).

3.1.5 Health services

There are 1061 hospitals and 153 Centers for disease prevention and control, 188 community health centers, 32 medical training institutions, 335 thousand health professionals and workers in the province(95).

So far, institutions and personnel for prevention and control of chronic diseases have been established gradually. Sentinel points and surveillance system on such diseases are also being set up. A number of epidemiological studies on chronic diseases have been conducted, which serve as the basis of planned intervention strategy.

In south of Jiangsu, Taicang is one of national demonstration areas for the prevention and control of chronic noncommunicable disease since the 1990s. Its working mode has been improved and generalized nationwide that integrated prevention and control network based on the community health centers, led by public health system, planed by local government.

3.2 Study design and population

This population-based cross-sectional study was conducted in both urban and rural areas, north and south in Jiangsu province, China. The study population was adults of both gender aged 35~74 years, who were residing in the province. Pregnant women, physically or mentally disabled person unable to follow simple questions and examinations were excluded.

3.3 Sampling method

3.3.1 Sample size calculation

Sample size of the present study was estimated based on the formula below:

$$N= (u_\alpha / \delta)^2 p (1-p)$$

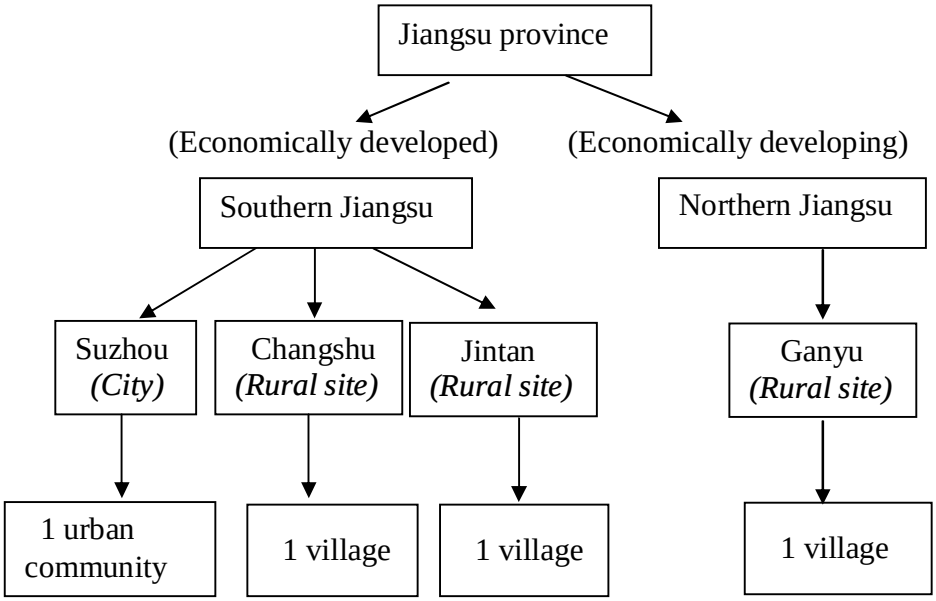
In this formula, 5% significance level (α=0.05) and 1% allowable error (δ =0.01) was assumed. Prevalence (p) of diabetes and metabolic syndrome among adults in Jiangsu province was estimated as 5.5% and 10%, respectively according to previous literatures available in Jiangsu or other areas with similar socioeconomic levels. So, the calculated sample size was 1997 and 3457, respectively. In addition, the sample size was added by 90% response rate to compensate for possible losses and refusals, leading to a modified sample size of 2219 and 3841 subjects, respectively.

The final sample size in the survey was 3914, which was larger than any one of theoretical values and could meet the requirement of analysis.

3.3.2 Sampling procedure

In the current study, four investigation sites were selected by multistage stratified cluster random sampling in the year of 2002 or so (initial time is different in different investigation sites, but within one year). The stratification factors are sex and age (35~74 years, 10 years difference between near age groups). Other demographic factors (urban/rural, rich/poor) were also be considered.

There were 4 steps in the process of multistage stratified cluster random sampling in the present study. ***Step 1***: 54 city districts and 52 counties in 13 prefectures in the province were divided into two groups based on the geographic and economic status, i.e. the north (low economic level) and south (high economic level). ***Step 2***: among them, 4 city district/counties were randomly selected, which were located both in south and north. ***Step 3***: All the urban communities or villages in each given area were listed with a random number, and the urban community/village with smallest number was selected respectively from each area. ***Step 4***: all of the residents aged 35-74 years without pregnancy, physically or mentally disabled who were living in the selected community/villages were put on the list. Sex and age group balance was cautiously considered in this step. Only one person was selected in each family to reduce the problem associated to clustering of some risk factors related to genetic predisposition, food habits and environmental factors. The sampling process was as follows:



Inclusion Criteria:

Both male and female residents aged 35~74 years who were randomly selected and also consented to participate into the baseline study in these sites in Jiangsu, China.

Exclusion criteria:

People who were not qualified by inclusion criteria were excluded from the study. And also, pregnant women, physically or mentally disabled person unable to follow simple questions and examinations were excluded.

3.4 Data collection

3.4.1 Pre-testing of questionnaires

Questionnaire was developed according to literatures and related experience. Before the start of large-scale survey, pre-testing of questionnaires was conducted among 50 subjects in local community to test the feasibility and reliability of the questionnaire.

A couple of questions in the questionnaire were modified or deleted in consideration of acceptance, relevance of the answers, time needed, and difficulty to answer, and so on. A rearranged questionnaire was used in the final study.

3.4.2 Interviewer-administered questionnaire

In local health service centers, face-to-face interviews were conducted by well-trained investigators. The questionnaire included general information, demographic variables, history of main diseases related to lifestyles, physical activity, etc. After finishing the interview, the investigators were also requested to give their general estimation (how reliable the collected information was) on the answers of the participants. And also, quality controller wrote down corresponding inspection results (qualified or not) as well.

General information, demographic features: it included name, sex, age, occupation, education, economics status, etc.

History of main diseases related: the participants were asked about some information regarding medical history (hypertension, diabetes, hyperlipidemia, obesity, and so on). History of drug medication was also involved.

Family history of diseases: it was defined as having a father, mother, bother, sister, son or daughter with diagnosed diseases with regard to hypertension, diabetes, hyperlipidemia, obesity, CVD, cancer, and so on

Lifestyle: it included smoking (smoking status, intensity, duration, type of tobacco used, second-hand smoking, etc), alcohol intake (drinking status, intensity, type of alcohol, experience of stopping drinking, etc), diet behaviors (frequency of various food and beverages consumption now and ten years ago)

Physical activity: it assessed frequency and intensity of physical activity, comparison with past time, and other people during both leisure time and work.

3.4.3 Biophysical assessment

Height, weight, waist and hip circumference, and blood pressure were included in this section. Height was measured by using well-mounted stadiometer without shoes to the nearest 0.1 cm. Weight was measured with light clothing and without shoes by an adjusted scale and recorded to the nearest 0.5 kg. The body mass index (BMI) was calculated as the weight (kg) divided by the square of the height (m). Height, weight, waist and hip circumference were taken twice. Waist circumference was measured at 1

cm above the level of navel at minimal respiration, and hip circumference at the level of maximum posterior extension of the buttocks with a tape which was calibrated weekly. Waist and hip circumference were recorded to the nearest 0.1 cm. Blood pressure was measured on the right arm in the sitting position for 3 times by using standard mercury sphygmomanometer, after 5 minutes of rest. The first and fifth Korotkoff sounds were recorded and the mean value of three measurements was used for analysis. All measurements were taken by trained health investigators in examination rooms.

3.4.4 Biochemical examination

All participants were kindly requested to take venous blood samples after fasting for at least 8 hours. The fasting time was further verified before the blood specimen was taken. Blood was collected in 3 different tubes. Aside from samples in EDTA tube, other samples in non-anticoagulant and fluoride tubes were centrifuged in local site within 3 hours to separate plasma. All samples were then refrigerated and stored at -20 ºC until laboratory assays could be done. Fasting plasma glucose (FPG), total triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) were measured in all of these blood samples. They were measured by Automatic HITACHI7020 Biochemical Analyzer. And other parameters like fructosamin, serum uric acid, lipoprotein a, Apo A, Apo B, C-reactive protein, leptin, insulin to be measured were measured in a subsample of participants. Quality control of the laboratory was assessed internally and externally.

3.4.5 Survey procedures

The protocol, the preparation of questionnaire and survey guideline was finished by Provincial Center for Disease Prevention and Control, and School of Public Health, Suzhou University. Uniform investigation plan was established. Identical questionnaire and other important survey equipments were provided by Provincial CDC.

After sampling, local centers for disease prevention and control were contacted in the four selected areas. Investigators together with health professionals were trained by

meeting in local CDC in each site. At the same time, selected subjects were informed to participate into the survey by local leaders in the communities or villages beforehand. Residents were also encouraged to participate by health professionals and workers. Normally, three days were spent on the fieldwork survey in each community or village.

On the first day, all of the questionnaires, equipments and materials needed were prepared and transported to local health service centers by CDC investigators.

On the second day, invited residents went to the local health service center after overnight fasting. In local health service centers, face-to-face interviews were conducted by well-trained investigators. Anthropometric test and blood sampling were also performed in the examination rooms at the time of interview.

On the third day, some residents who didn't attend the survey on the previous day due to various causes such as employment, not fasting, etc. were invited to participate again. And also, the information collected by questionnaire, body examination was checked with the participants in case of doubt.

During the fieldwork survey, all the organizers or investigators in the study discussed fieldwork problems they met by meeting or group discussion.

3.4.6 Health personnel training and field work supervision

These two components were important parts of survey to guarantee the quality. Investigators were selected from personnel working in local CDC or health service centers with experience of epidemiological survey. They were trained by meeting in local CDC in each site. The background, objectives, the content of investigation, requirement of interview and examination were introduced in the meeting. And also, the guideline and handbook of survey were distributed. After the training, qualified investigators were allowed to attend the survey.

The fieldwork was supervised by professionals from quality control group with regard to the data collection, checking lab results, data entry and management, checking of death causes. Errors found could be corrected.

3.5 Categorizations of metabolic syndrome, diabetes and IFG

In the present study, three different diagnostic criteria including the WHO, IDF and modified ATP III definitions(31-33) were all used to identify participants with metabolic syndrome in order for comparison and judgment. Detailed measurements and categorical cutoff points for each definition were shown in Table 1.1.

According to the latest recommendations of the American Diabetes Association(11), participants were defined as having diabetes based on:

1. Their fasting plasma glucose levels≥7.0 mmol/l.
2. If they answer "yes" to the question about whether they were ever told by a doctor that they had diabetes other than gestation period.

Likewise, impaired fasting glucose (IFG) was defined when:

1. Fasting plasma glucose level between 5.6 to <7.0 mmol/l, and also
2. Subjects reporting to use any glucose-lowering agents were considered as diabetic.

3.6 Statistical methods

3.6.1 Data management

All of the information collected by questionnaire, medical examination and biochemical analysis were entered into computer by using Epidata 3.0. The importing procedure is congruously provided by Provincial CDC. All collected data were stored in a computer database. A trained team checked the recorded information for missing values (which should be avoided during fieldwork) and data entry errors.

3.6.2 Data handling

The definitions and classifications of various measurements can be found in Table 1.1. Numerical data were described by mean and standard deviation, compared by t test if

they were normally distributed. Categorical data were expressed as frequency and percentage and compared by Chi-square test or non-parametric tests between different subgroups. $P<0.05$ was considered significance and probability values were two-sided. Data analyses were conducted mainly using the SAS System (version 8.1, SAS Institute, Cary, NC).

The prevalence of diseases was calculated and standardized by using the data of the 5th National Census (in the year of 2000)(100). A multivariable logistic regression was performed to identify associated factors for diabetes and metabolic syndrome (selection=stepwise, sle=0.1, sls=0.1). Logistic model was also used for controlling potential confounders such as sex, age, BMI, smoking, alcohol drinking, educational level, and family history of chronic diseases based on previous publications. The multivariate-adjusted ORs and 95% confidence intervals were presented. Agreement between different MetS definitions was evaluated by the kappa statistic (poor, $\kappa \leq 0.20$; fair, $\kappa = 0.21$ to 0.40; moderate, $\kappa = 0.41$ to 0.60; substantial, $\kappa = 0.61$ to 0.80; very good, $\kappa > 0.80$)(101).

Relationship between fasting plasma glucose level and other parameters were analyzed by simple and partial correlation analysis. Since the distribution of CRP was skewed, a logarithmic transformation (log 10) was performed and used in simple and partial correlation analysis. Potential confounders such as age, area, BMI, education, family history of diabetes, smoking, drinking, and sedentary lifestyle were adjusted in multiple models. The international classification of adult BMI categories according to World Health Organization (WHO) was made as underweight (<18.5 kg/m2), normal weight (18.5–24.9 kg/m2), overweight (25–29.9 kg/m2) and obesity (30 kg/m2 or greater)(102).

3.7 Ethical clearance

Ethical clearance was obtained from the Norwegian Research Ethical Committee. Approval to conduct this study was also obtained from both Jiangsu Provincial CDC and local official institutions. The objectives of the study and methods to be used were

explained sufficiently to the participants who were treated with respect for their dignity. They were reassured about the confidentiality of data. Folding screens will be used to isolate subjects. Male and female participants were arranged to stay in different separate rooms when conducting anthropometric measurements. In consideration of safety for both subjects and doctors, disposable hypodermic syringes, gloves and other necessities were used while taking blood samples.

The investigation initiated only after getting written informed consent from the participants of both sexes (shown in appendix). They were never pushed to do it. All the participants were free to quit from the research at any time. The questionnaires and laboratory documents were kept at Jiangsu Provincial CDC securely. Likewise, the blood specimens were frozen and stored. All of the tests on blood were done for research purpose. Due to the need of follow-up, the contact information like names and address were kept in the research files. However, they were kept away from data and handled by other unrelated researchers. All of the information will have the name and address removed so that the participants could not be recognized from it when the follow-up research is finished.

The written results of medical examination were distributed and explained to participants themselves in time. They were free to discuss their health results with their doctors. And also, they were encouraged to raise health questions and the questions would be answered individually. Medical suggestions (nutrition, lifestyle modification, etc) were also delivered. Anyway, the subjects and target population would benefit from the research potentially although our project didn’t provide intervention or medication directly. Those who were found as diabetic or MS in the research were referred to the healthcare centers/hospitals.

4. RESULTS

4.1 Basic description of study sample

4.1.1 Description of baseline characteristics

Table 4.1 Baseline characteristics of 3914 study subjects by gender from Jiangsu Province, China

Variables	Men (n=1748)	Women (n=2166)	Total (n=3914)
Continuous variables			
Age (years)	54.3±10.9	53.0±10.8**	53.5±10.9
Waist circumference (cm)	80.7±9.8	79.3±9.6**	79.9±9.7
Hip circumference (cm)	93.7±7.5	94.3±7.4*	94.0±7.5
WHR	0.86±0.07	0.84±0.07**	0.85±0.07
BMI (kg/m^2)	23.1±3.4	23.8±3.4**	23.5±3.4
SBP (mmHg)	127.9±20.2	125.5±20.6**	126.6±20.5
DBP (mmHg)	79.6±11.0	76.9±10.4**	78.1±10.7
FPG (mmol/l)	5.43±1.46	5.60±1.67**	5.52±1.58
Cholesterol (mmol/l)	5.27±1.24	5.45±1.37**	5.37±1.32
TG (mmol/l)	1.78±1.28	1.84±1.09	1.82±1.18
HDLC (mmol/l)	1.32±0.47	1.36±0.41*	1.34±0.44
LDLC (mmol/l)	3.17±1.07	3.20±1.09	3.19±1.08
lipoprotein a (mg/l)	463.8±235.2	490.3±204.7**	478.6±219.1
Apo A (g/l)	1.79±0.62	1.92±0.58**	1.86±0.60
Apo B (g/l)	0.71±0.27	0.76±0.28**	0.74±0.28
Categorical variables			
Education**			
Illiterate	202 (11.6)	930 (42.9)	1132 (28.9)
Primary school	615 (35.2)	622 (28.7)	1237 (31.6)
Middle school	792 (45.3)	576 (26.6)	1368 (35.5)
Junior college/university	139 (8.0)	38 (1.8)	177 (4.5)
Income (RMB Yuan/year) **			
<6000	1091 (62.4)	1490 (68.8)	2581 (65.9)
6000-15000	532 (30.4)	589 (27.2)	1121 (28.6)
15000-25000	90 (5.2)	67 (3.1)	157 (4.0)
≥25000	35 (2.0)	20 (0.9)	55 (1.4)
Smoking (yes)	1194 (68.3)	81 (3.8) **	1275 (32.6)
Alcohol drinking (yes)	983 (56.2)	130 (6.0)**	1113 (28.5)
Sedentary lifestyle (yes)	246 (18.0)	291 (16.8)	537 (17.3)

Data were mean ± SD or n (%); Smoking variable has 6 missing value, alcohol drinking has 2 missing value, and sedentary lifestyle variable has 814 missing value; the value in men was significantly different from that in women at *p<0.05, **p<0.01 by student t test or $\chi 2$ test.

The baseline characteristics of 3914 study subjects were shown in table 4.1. The mean ages of men and women were 54.3 and 53.0 years, respectively. Age, waist circumference, waist-to-hip ratio, systolic blood pressure, diastolic blood pressure, smoking and alcohol drinking rate were significantly higher in men than those in women, while hip circumference, BMI, fasting plasma glucose, plasma cholesterol, HDLC, lipoprotein a, Apo A and Apo B were significantly lower in men than those in women. Moreover, the proportions of different strata in education level and yearly income were also significantly different between men and women by using a Cochran-Mantel-Haenszel chi-squared test.

4.1.2 Mean glucose concentrations in subgroups

As shown in Table 4.2, fasting plasma glucose concentration increased with age, BMI status and yearly income in both sexes. Women had significantly higher glucose level than men after 55 years old ($p<0.01$). And also, overweight women had higher glucose level than overweight men. The same difference was observed in low and middle income families and in subjects with illiterate and primary education level.

Table 4.2 Mean glucose concentrations in different subgroups in 3914 study subjects from Jiangsu Province, China

	Men	Women	Total
N	1748	2166	3914
Age group (years)			
35-44	5.23±1.64	5.25±1.26	5.24±1.43
45-54	5.41±1.50	5.52±1.49	5.46±1.50
55-64	5.54±1.29	5.83±1.91**	5.70±1.67
65-74	5.68±1.37	5.94±1.93**	5.74±1.69
BMI status			
Underweight	5.22±0.84	5.44±2.05	5.33±1.54
Normal	5.42±1.48	5.50±1.62	5.46±1.56
Overweight	5.47±1.44	5.81±1.72**	5.67±1.63
Obesity	5.86±1.92	5.84±1.42	5.85±1.60
Income (RMB Yuan/year)			
Low (<6000)	5.39±1.41	5.51±1.60*	5.46±1.53
Middle (6000-15000)	5.50±1.55	5.76±1.56**	5.63±1.56
High (≥15000)	5.56±1.47	6.11±2.87	5.78±2.16
Education			
Illiterate	5.33±1.06	5.61±1.60**	5.56±1.52

Primary school	5.50±1.60	5.76±2.00*	5.63±1.82
Middle school	5.39±1.41	5.44±1.37	5.41±1.39
Junior college/university	5.48±1.57	5.40±0.74	5.41±1.44

* p<0.05, ** p<0.01 tested by student t test.

4.1.3 Other parameters

Some inflammation, adipocytokines variables was shown in Table 4.3. Women had significantly higher leptin level than men (p<0.001). And also, interleukin-6 concentration was higher in women than in men (p<0.05), while levels of C-reactive protein, Von Willebrand factor were lower in women (p<0.05).

Table 4.3 Mean value and standard deviation of other parameters among 269 subjects by gender

Variables	Men	Women	P value
CRP (mg/l)	2.70 (1.70-4.60)	2.50 (1.70-4.30)	0.035
Leptin (ng/ml)	1406.20 (1015.90)	2561.30 (793.66)	<0.001
Insulin (uIU/ml)	38.70 (18.25)	35.05 (14.03)	0.088
HOMA-IR	9.41 (5.60)	8.17 (4.71)	0.054
TPA	11.84 (7.41-25.65)	13.10 (7.94-23.37)	0.771
TNF-α (pmol/L)	10.74 (8.67)	9.64 (13.31)	0.414
PAI-1	43.13 (23.68)	46.75 (24.53)	0.238
Fibrinogen	217.18 (93.20)	206.28 (104.19)	0.391
IL-6 (pg/ml)	0 (0-0)	0 (0-0)	0.012
Endothelin-1 (ng/mL)	86.28 (47.80)	78.66 (40.75)	0.167
VWF	140.14 (131.35)	107.18 (93.98)	0.030

Data of normal distribution were presented as mean (standard deviation), tested by student t test; data of abnormal distribution were presented as median (interquartile range), tested by Wilcoxon test.

4.2 Prevalence and associated factors for diabetes and IFG

4.2.1 Prevalence of diabetes, IFG and hyperglycemia

The overall prevalence of diabetes was 7.7%. The prevalence became little lower after age standardization (6.8%). The diabetes was more common in female than in male (p<0.05). The age-standardized prevalence of diabetes was higher in women than in men (7.6% vs. 5.9%).

The overall and age-standardized prevalence of IFG was 23.1% and 21.0% respectively. It was more common in female than in male (p<0.05). The age-standardized prevalence

of IFG was higher in women than in men (22.7% vs. 18.9%).

The overall and age-standardized prevalence of hyperglycemia was 30.7% and 27.8% respectively. Like diabetes and IFG, hyperglycemia was more common in female than in male as well ($p<0.01$). The age-standardized prevalence of diabetes was higher in women than in men (30.3% vs. 24.8%).

Prevalence of diabetes, IFG and hyperglycemia increased significantly with age, yearly income, and BMI status, although IFG and hyperglycemia decreased slightly in high yearly income group (Table 4.4). Overall, women at age of 65-74 years or with obesity had the highest rate of abnormal glucose level regardless of which type it was (diabetes, IFG or hyperglycemia).

Table 4.4 Prevalence of diabetes, IFG and hyperglycemia in 3914 participants aged 35-74 years in Jiangsu, China

	N	Diabetes (%)	IFG (%)	Hyperglycemia (%)
Total	3914	7.7	23.1	30.7
Age-Standardized	3914	6.8	21.0	27.8
Sex				
Male	1748	6.6*	21.4*	28.0**
Age-Standardized, male	1748	5.9	18.9	24.8
Female	2166	8.6	24.4	33.0
Age-Standardized, female	2166	7.6	22.7	30.3
Age group (years)				
35-44	1012	4.1**	15.4**	19.5**
45-54	1074	7.0	20.6	27.6
55-64	1097	9.6	28.6	38.2
65-74	731	10.9	28.9	39.8
Area				
Urban	762	7.1	26.1*	33.2
Rural	3152	7.8	22.3	30.1
Income				
Low (<6000)	2581	7.1*	21.2**	28.3**
Middle (6000-15000)	1121	8.5	27.1	35.6
High (≥15000)	212	10.4	24.5	34.9
BMI status				
Underweight	209	4.3**	18.2**	22.5**
Normal	2551	7.1	21.0	28.1
Overweight	1002	9.1	28.0	37.1
Obesity	152	12.5	31.6	44.1

Age-adjusted by direct standardization using the 2000 Chinese census population; Hyperglycemia= diabetes+ IFG; * p<0.05, ** p<0.01, by using $\chi 2$ test between two categories, or $\chi 2$ test for trend among all categories.

4.2.2 Risk factors for diabetes

To identify the associated factors of diabetes, univariate and multivariate logistic regression were used. Sex, age, yearly income, education level, BMI status, smoking and family history of diabetes were showed to be significant predictors for the occurrence of diabetes in univariate analysis (Table 4.5).

Table 4.5 Multivariate regression models for the relationship between diabetes and selected sociodemographic, behavioral variables in 3860 participants aged 35-74 years from Jiangsu, China

	OR (95% CI)[1]	*p*	OR (95% CI)[2]	*p*
Sex				
Men	1.00 (referent)		1.00	
Women	1.33 (1.05–1.70)	0.019	1.34 (0.93–1.94)	0.120
Age group (years)				
35-44	1.00		1.00	
45-54	1.78 (1.20–2.63)	0.003	1.90 (1.27–2.84)	0.002
55-64	2.51 (1.73–3.64)	<0.001	2.53 (1.70–3.75)	<0.001
65-74	2.91 (1.97–4.30)	<0.001	3.34 (2.17–5.13)	<0.001
Area				
Rural	1.00		1.00	
Urban	0.90 (0.66–1.22)	0.486	0.69 (0.48–1.00)	0.047
Income				
Low (<6000)	1.00		1.00	
Middle (6000-15000)	1.21 (0.93-1.56)	0.155	1.27 (0.95-1.69)	0.104
High (≥15000)	1.51 (0.95-2.40)	0.084	1.86 (1.13-3.01)	0.015
Education				
<middle school	1.00		1.00	
≥Middle school	0.69 (0.54-0.89)	0.004	0.90 (0.65-1.24)	0.512
BMI status				
Underweight	0.59 (0.30-1.16)	0.126	0.57 (0.28-1.13)	0.108
Normal	1.00		1.00	
Overweight	1.30 (1.00-1.69)	0.050	1.18 (0.90-1.56)	0.229
Obesity	1.86 (1.12-3.08)	0.016	1.71 (1.02-2.89)	0.044
Smoking				
Never	1.00		1.00	
Former	1.29 (0.72-2.33)	0.396	1.33 (0.68-2.59)	0.403
Current	0.73 (0.55-0.96)	0.025	0.86 (0.59-1.27)	0.459
Alcohol drinking				
Never	1.00		1.00	
Former	1.01 (0.43-2.34)	0.990	0.96 (0.39-2.36)	0.928
Current	0.86 (0.65-1.14)	0.290	1.12 (0.79-1.58)	0.525
Family history of diabetes				

No	1.00		1.00	
Yes	3.84 (2.67-5.51)	<0.001	4.39 (2.99-6.46)	<0.001
Family history of hypertension				
No	1.00		1.00	
Yes	1.06 (0.82-1.37)	0.643	0.90 (0.69-1.18)	0.447

1 crude odds ratio, 2 adjusted odds ratio for sex, age, area, yearly income, education, BMI status, smoking, alcohol drinking, family history of diabetes, and family history of hypertension.
OR (odds ratio), 95% CI (95% confidence interval)
Physical activity: exercise everyday or sedentary<8h.

Age, yearly income, BMI status and family history of diabetes remained significant after adjusted for a number of possible confounding variables in multivariate analysis. For example, the risk for developing diabetes was almost 3.3 times higher above in the age of 65 years compared to the younger age group 35-44 years. Family history of diabetes was the prime predictor of diabetes in the study population. Person with family history of diabetes was 3-6.5 times more likely to have diabetes than one without the history.

However, BMI was found as the strongest modifiable factor for the development of diabetes. Overweight and obesity were important risk factors for diabetes, while underweight as negatively associated with diabetes independent of sex, age, yearly income and other risk factors in the study population. Obese people had almost two times higher risk for development of diabetes than people with normal weight.

4.3 Prevalence and determinants for metabolic syndrome

4.3.1 Prevalence and distribution of MetS components

Table 4.6 showed the prevalence of MetS components defined by modified ATP III definitions. High blood pressure was the most prevalent components of MetS (45.2%), followed by elevated TG (40.1%) and low HDLC (40.1%) in middle-aged and elderly Chinese in Jiangsu province.

Table 4.6 Prevalence of MetS components defined by modified ATP III definition, in 3914 people aged 35-74 years

	N	Central obesity (%)	High TG(%)	Low HDLC(%)	High BP (%)	High FPG(%)
Total	3914	33.2	40.1	40.1	45.2	30.7

Sex						
Male	1748	17.9	36.9	29.1	49.1	28.0
Female	2166	45.5	42.7	49.0	42.0	32.9
Age group (years)						
35-44	1012	30.3	35.7	48.4	28.2	19.5
45-54	1074	31.3	35.4	43.0	37.5	27.6
55-64	1097	36.7	44.9	36.0	56.4	38.2
65-74	731	34.8	45.8	30.6	63.1	39.7
Area						
Urban	762	34.0	36.2	68.9	40.2	33.2
Rural	3152	33.0	41.0	33.2	46.4	30.1
Income						
Low (<6000)	2581	32.4	37.1	39.6	45.1	28.2
Middle (6000-15000)	1121	35.6	45.1	42.5	44.8	35.6
High (≥15000)	212	30.2	49.5	34.9	48.6	34.9
BMI status						
Normal	2551	15.9	32.9	36.2	39.1	28.1
Overweight	1002	74.3	59.7	50.6	60.0	37.1
Obesity	152	96.7	63.8	55.3	77.0	44.1

The prevalence of all MetS components except increased blood pressure was higher in women in the study population. Prevalence of all MetS components unanimously increased with BMI status (Table 4.4 and Figure 4.1).

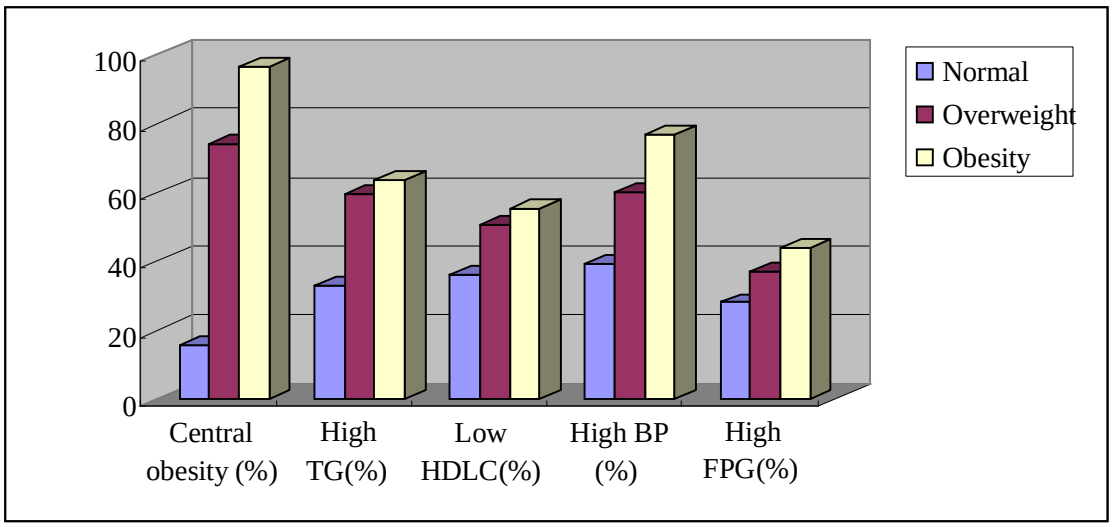


Figure 4.1 Prevalence of MetS components by different level of BMI in 3914 adults

4.3.2 Prevalence of overweight/obesity defined by adult BMI

According to WHO standard, there were 1002 overweight subjects and 152 obese subjects in the 3914 individuals of the study sample. The prevalence of overweight, obesity, and overweight together with obesity was 25.6%, 3.9% and 29.5% all together (Table 4.7). They were more popular in women and in urban area ($p<0.01$). People having higher family income also had higher rates.

Table 4.7 Prevalence of overweight and obesity defined by BMI, among 3914 people aged 35-74 years in different subgroups

	N	Overweight (%)	Obesity (%)	Overweight + Obesity (%)
Total	3914	25.6	3.9	29.5
Sex				
Male	1748	22.4**	2.9**	25.3**
Female	2166	28.2	4.7	32.9
Age group (years)				
35-44	1012	27.1	4.6	31.7
45-54	1074	23.9	3.3	27.2
55-64	1097	27.5	3.6	31.1
65-74	731	23.1	4.2	27.4
Area				
Urban	762	30.7**	4.7**	35.4**
Rural	3152	24.4	3.7	28.1
Income				
Low (<6000)	2581	22.9**	3.4*	26.2**
Middle (6000-15000)	1121	31.1	4.9	36.0
High (≥15000)	212	29.7	4.7	34.4

* $p<0.05$, ** $p<0.01$, by using $\chi 2$ test between male/female or urban/rural group, or $\chi 2$ test for trend among all categories.

4.3.3 Prevalence of metabolic syndrome

The overall and adjusted overall prevalence of metabolic syndrome defined by WHO criteria was 14.1% and 12.3%, respectively (data not shown). The metabolic syndrome was more common in female than in male ($\chi 2=22.8$, $p<0.001$). The adjusted prevalence of metabolic syndrome was also higher in women than in men (14.5% vs. 9.7%, $p<0.001$).

As presented in Table 4.8, the overall prevalence of metabolic syndrome defined by IDF criteria was 23.1%. The prevalence became little lower after age standardization (21.8%). It was more common in female than in male ($p<0.01$). The adjusted prevalence of

metabolic syndrome was higher in women than in men (27.9% vs. 13.8%).

The overall prevalence of metabolic syndrome defined by modified ATP III criteria was 31.5%. The standardized prevalence was 30.5%. The metabolic syndrome was more common in female than in male ($p<0.01$). The adjusted prevalence of metabolic syndrome was higher in women than in men (34.2% vs. 24.0%).

Table 4.8 Prevalence of MetS in 3914 study subjects from Jiangsu Province by the IDF and modified ATP III definitions, respectively

	n	Prevalence [a] %(95% CI)	Prevalence [b] %(95% CI)
Overall	3914	23.1 (21.7-24.4)	31.5 (30.1-33.0)
Overall adjusted*		21.8	30.5
Male	1748	12.9 (11.4-14.5) †	23.5 (21.5-25.5) †
Male adjusted*		13.8†	24.0†
Age group (years)			
35-44	418	16.5 (13.0-20.1) ‡	25.6 (21.4-29.8)
45-54	473	12.7 (9.7-15.7)	23.5 (19.7-27.3)
55-64	494	11.3 (8.5-14.1)	22.7 (19.0-26.4)
65-74	363	11.3 (8.0-14.6)	22.3 (18.0-26.6)
BMI status			
Normal	1196	2.6 (1.7-3.5) §	13.0 (11.1-15.0) §
Overweight	391	38.9 (34.0-43.7)	52.9 (48.0-57.9)
Obesity	51	82.4 (71.9-92.8)	82.4 (71.9-92.8)
Female	2166	31.2 (29.3-33.2)	38.0 (36.0-40.0)
Female adjusted*		27.9	34.2
Age group (years)			
35-44	594	18.4 (15.2-21.5) §	22.9 (19.5-26.3) §
45-54	601	24.6 (21.2-28.1)	31.1 (27.4-34.8)
55-64	603	42.1 (38.2-46.1)	50.1 (46.1-54.1)
65-74	378	44.8 (39.8-49.9)	53.8 (48.7-58.9)
BMI status			
Normal	1355	15.7 (13.7-17.6) §	25.2 (22.9-27.5) §
Overweight	611	62.5 (58.7-66.4)	64.7 (60.9-68.4)
Obesity	101	80.2 (72.4-88.0)	80.2 (72.4-88.0)

a prevalence by IDF definition, b prevalence by modified ATP III definition.
* Adjusted by direct standardization to the gender and age distribution (categorized as 35-44, 45-54, 55-64, 65-74 years) of the 2000 Chinese census population.
† $p<0.01$, $\chi 2$ test between male versus female group.
‡ $p<0.05$, $\chi 2$ test for trend among different age groups.
§ $p<0.01$, $\chi 2$ test for trend among different age groups or BMI status.
CI=confidence interval; BMI=body mass index.

The prevalence of MetS significantly increased with age in female group independent of definitions. And also, the prevalence of MetS significantly increased with BMI status for both sexes and both definitions, which was shown in Table 4.8.

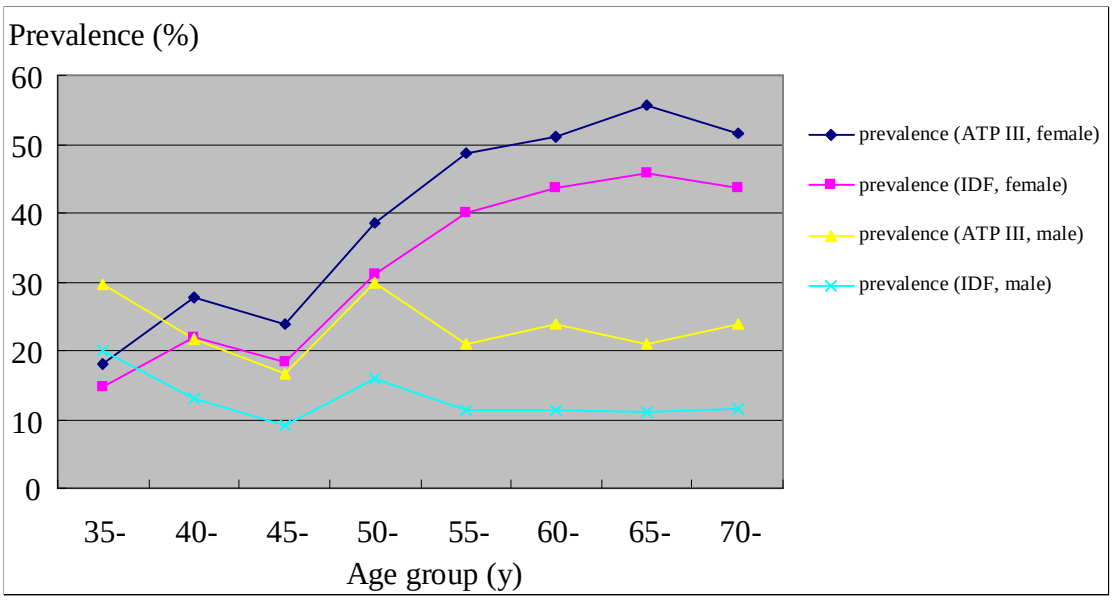


Figure 4.2 Prevalence of MetS in different sex and age groups (5 years interval) in 3914 study subjects from Jiangsu Province

Association between prevalence of MetS and age was displayed in Figure 4.2. The prevalence of MetS significantly increased with age (5 years interval) in female group by both definitions (p for trend<0.001). Additionally, female in the age of 65-69 years had the highest rate of metabolic syndrome (Figure 4.2).

4.3.4 Combination type of MetS components

Because metabolic syndrome was a cluster of various factors, which kind of congregation was popular deserved discussion in a given population. All of the 5 components and their categorizations were identical in IDF and modified ATP III criteria. As shown in Table 4.9, the most common combination of 3 out of 5 MetS components in the sample of 3914 subjects was central obesity + high TG + low HDLC, followed by high TG + low HDLC + high blood pressure.

Table 4.9 Combination type of 3 out of 5 MetS components in the sample of 3914 subjects

Combination type	Frequency	Percent (%)
1, 2, 3	112	2.86
1, 2 ,4	93	2.38
1, 2, 5	50	1.28
1, 3, 4	93	2.38
1, 3, 5	21	0.54
1, 4, 5	51	1.30
2, 3, 4	110	2.81
2, 3, 5	49	1.25
2, 4, 5	91	2.32
3, 4, 5	32	0.82

In this table, 1 represented central obesity. 2, 3, 4, 5 represented high TG, low HDLC, high blood pressure and high FPG, respectively.

The most common combination of 4 out of 5 MetS components in the sample of 3914 subjects was central obesity + high TG + high blood pressure+ high FPG (136, 3.47%), followed by central obesity + high TG + low HDLC + high blood pressure (129, 3.30%) (data not shown).

There were 121 persons (28 males, 93 females, 3.09% overall) in the study population who had all the five MetS components with them (data not shown).

4.3.5 Determinants of metabolic syndrome

13 potential associated factors for metabolic syndrome were classified and given with corresponding value, except age and BMI which were regarded as continuous variable. Age and BMI changed per unit of standard deviation. Detailed information was shown in Table 4.10.

Table 4.10 Value assignment for potential associated factors

Variable	Classification and value
Sex	male=1, female=2
Age	per 10.9 years
Area	rural=0, urban=1
Education level	<middle school=0, ≥Middle school=1
Yearly income	low (<6000)=1, middle (6000-15000)=2, high (≥15000)=3

BMI	per 3.4 kg/m2
Family history of hypertension	no=0, yes=1
Family history of diabetes	no=0, yes=1
Smoking status	no=0, current smoking=1, ever smoking=2
Second-hand smoking	no=0, yes=1
Alcohol drinking	no=0, current drinking=1, ever drinking =2
Tea consumption	≥1 cup of tea everyday=1, no=0
Sedentary lifestyle	exercise everyday or sedentary<8h=0, otherwise=1

All the variables in Table 4.10 were considered in multivariate logistic regression (selection=stepwise, sle=0.1, sls=0.1). Only significant factors ($p<0.05$) by multivariate logistic regression analysis were shown in Table 4.11 and Table 4.12.

Gender was found to be significant risk factors for metabolic syndrome independent of definition in total analysis including both men and women (OR=1.44, p=0.002).

In men (Table 4.11), BMI status was found to be significant risk factor for metabolic syndrome independent of definition. Especially, the risk of having metabolic syndrome defined by IDF was 8.3 times as BMI increased per unit of 3.4 kg/m2. Age and family history of diabetes were risk factors for metabolic syndrome defined by WHO and modified ATP III criteria. And also, smoking was identified as risk factors for metabolic syndrome defined by WHO and IDF criteria. Sedentary lifestyle was regarded as risk factors for metabolic syndrome defined by IDF and modified ATP III criteria.

Habit of tea consumption for modified ATP III MetS was found as protective factor in men.

Moreover, higher yearly income for WHO MetS, living in urban area, family history of hypertension for modified ATP III MetS were also identified as risk factors respectively in man participants.

Table 4.11 Odds ratio for association between sociodemographic and lifestyle variables and metabolic syndrome by multivariate logistic regression in 1316 men

Significant variable	Adjusted OR* (95% CI)	*p*
MetS [a]		
Age (per 10.9 years)	1.56 (1.31-1.86)	<0.001
Yearly income	1.31 (1.02-1.66)	0.032
BMI (per 3.4 kg/m2)	1.50 (1.28-1.76)	<0.001
Family history of diabetes	2.88 (1.61-5.14)	<0.001
Smoking status	1.34 (1.02-1.76)	0.035
MetS [b]		
Area	1.57 (1.00-2.44)	0.049
BMI (per 3.4 kg/m2)	8.29 (6.24-10.99)	<0.001
Smoking status	1.47 (1.05-2.05)	0.024
Sedentary lifestyle	1.79 (1.14-2.82)	0.012
MetS [c]		
Age (per 10.9 years)	1.25 (1.08-1.45)	0.004
Area	2.09 (1.46-2.98)	<0.001
BMI (per 3.4 kg/m2)	3.79 (3.15-4.56)	<0.001
Family history of diabetes	1.89 (1.04-3.44)	0.038
Family history of hypertension	1.42 (1.00-2.01)	0.049
Sedentary lifestyle	1.47 (1.02-2.11)	0.038
Tea consumption	0.70 (0.51-0.96)	0.028

a prevalence by WHO definition; b prevalence by IDF definition; c prevalence by modified ATP III definition. * Adjusted for all the variables in Table 4.10.

In women (Table 4.12), age, BMI status and family history of hypertension were found to be significant risk factors for metabolic syndrome independent of definition. Especially, the risk of having metabolic syndrome defined by IDF was 6.2 times as BMI increased per unit of 3.4 kg/m2. Family history of diabetes was risk factor for metabolic syndrome defined by WHO and modified ATP III criteria. And also, smoking was identified as risk factors for metabolic syndrome defined by IDF and modified ATP III criteria.

Higher education level was found as protective factor for WHO-definition MetS in women.

Moreover, higher yearly income was also identified as risk factor for WHO MetS, the same as living in urban area for modified ATP III MetS, in female participants.

Table 4.12 Odds ratio for association between sociodemographic and lifestyle variables and metabolic syndrome by multivariate logistic regression in 1651 women

Significant variable	Adjusted OR* (95% CI)	*p*
MetS [a]		
Age (per 10.9 years)	1.61 (1.38-1.88)	<0.001
Education level	0.67 (0.47-0.94)	0.021
Yearly income	1.49 (1.18-1.87)	<0.001
BMI (per 3.4 kg/m2)	1.46 (1.29-1.66)	<0.001
Family history of diabetes	1.68 (1.02-2.75)	0.041
Family history of hypertension	1.46 (1.08-1.98)	0.014
MetS [b]		
Age (per 10.9 years)	1.97 (1.70-2.27)	<0.001
BMI (per 3.4 kg/m2)	6.18 (5.10-7.49)	<0.001
Family history of hypertension	1.41 (1.03-1.94)	0.033
Smoking status	1.81 (1.06-3.10)	0.031
MetS [c]		
Age (per 10.9 years)	1.97 (1.73-2.24)	<0.001
Area	1.34 (1.02-1.77)	0.038
BMI (per 3.4 kg/m2)	3.61 (3.11-4.20)	<0.001
Family history of diabetes	1.66 (1.01-2.72)	0.045
Family history of hypertension	1.56 (1.16-2.10)	0.003
Smoking status	2.10 (1.24-3.56)	0.006

a prevalence by WHO definition; b prevalence by IDF definition; c prevalence by modified ATP III definition. * Adjusted for all the variables in Table 4.10.

4.4 Agreement for different definitions of metabolic syndrome

Table 4.13 Agreement between the WHO, IDF and modified ATP III criteria in diagnosing metabolic syndrome

		Modified ATP III			Kappa (95% CI)
		+	-	Total	
WHO	+	416	134	550	0.34 (0.31-0.37)
	-	818	2546	3364	
	Total	1234	2680	3914	
IDF	+	902	0	902	0.79 (0.77-0.81)
	-	332	2680	3012	
	Total	1234	2680	3914	
		WHO			
		+	-	Total	
IDF	+	289	613	902	0.27 (0.24-0.31)
	-	261	2751	3012	
	Total	550	3364	3914	

From table 4.13, substantial agreement (κ=0.79) was found between IDF and modified ATP III definitions. They agreed with each other with highest degree among three comparisons. All of the positive subjects, who were diagnosed by IDF definition, were also modified ATP III definition positive. Fair agreement (κ=0.34) was found between WHO and modified ATP III definitions. And also fair agreement (κ=0.27) was observed between WHO and IDF definitions, and it was the lowest one.

4.5 Weight gain

Table 4.14 Logistic model relating 10-year BMI change to hyperglycemia, MetS by 3 definitions, stratified by BMI status 10 years ago among 2343 subjects in Jiangsu

	Cases	OR[1] (95% CI)	P[1]	OR[2] (95% CI)	P[2]
Hyperglycemia					
Underweight	20	1.01 (0.82-1.24)	0.951	1.04 (0.83-1.30)	0.731
Normal	329	1.11 (1.06-1.16)	<0.001	1.12 (1.06-1.17)	<0.001
Overweight	129	1.05 (0.97-1.13)	0.184	1.04 (0.96-1.12)	0.367
Obesity	14	0.84 (0.67-1.04)	0.111	0.88 (0.69-1.13)	0.316
MetS [a]					
Underweight	4	1.08 (0.72-1.63)	0.711	1.01 (0.61-1.66)	0.971
Normal	113	1.12 (1.05-1.20)	<0.001	1.16 (1.08-1.25)	<0.001
Overweight	78	1.03 (0.95-1.13)	0.467	1.02 (0.93-1.12)	0.670
Obesity	8	0.87 (0.68-1.12)	0.285	0.92 (0.67-1.25)	0.579
MetS [b]					
Underweight	4	2.69 (1.41-5.12)	0.003	-	-
Normal	273	1.55 (1.46-1.65)	<0.001	1.70 (1.58-1.83)	<0.001
Overweight	188	1.39 (1.27-1.52)	<0.001	1.44 (1.31-1.59)	<0.001
Obesity	24	1.30 (1.02-1.65)	0.032	1.28 (0.94-1.75)	0.118
MetS [c]					
Underweight	15	1.42 (1.12-1.79)	0.004	1.42 (1.08-1.85)	0.011
Normal	431	1.41 (1.34-1.49)	<0.001	1.48 (1.39-1.56)	<0.001
Overweight	222	1.29 (1.19-1.40)	<0.001	1.31 (1.21-1.43)	<0.001
Obesity	25	1.26 (1.00-1.59)	0.051	1.24 (0.93-1.65)	0.140

a prevalence by WHO definition; b prevalence by IDF definition; c prevalence by modified ATP III definition. Hyperglycemia=IFG + diabetes; 1 crude odds ratio and p value; 2 odds ratio and p value adjusted for sex, age, area, yearly income, education, smoking, alcohol drinking, family history of diabetes.1 unit change in BMI was 2.9 kg for a 1.7-m-tall person.

Additional analysis on Association between 10-year weight gain and the risk of hyperglycemia and metabolic syndrome by 3 definitions was shown in Table 4.14. Due to the number of observations in each stratum, hyperglycemia instead of diabetes was considered here. Weight gain was calculated as the difference between weight at survey

and weight ten years ago. In consideration of different height of subjects, it was change into 10-year BMI change in the model.

Table 4.14 further indicated weight gain was particularly risk factor for each disease among originally normal weight population ($p<0.001$). For person with normal weight 10 years ago, if BMI increase 1 unit, the risk of developing MetS by IDF definition would have a 1.7-fold average increase.

4.6 Analysis on nontraditional risk factors

4.6.1 Simple and partial correlation

By simple correlation analysis, fasting glucose level was found positively correlated with BMI, waist circumference, triglyceride, HDLC, systolic blood pressure, fructosamin, HOMA-IR, interleukin-6 in both sexes. After adjusted for age, area, education, family history of diabetes, smoking, drinking, and sedentary lifestyle, these correlations except HDLC in male still remained significant. Further adjustment for BMI didn't weaken the relationship between glucose level and triglyceride, HDLC in female, fructosamin, HOMA-IR, interleukin-6 (Table 4.15).

Fasting plasma glucose appeared to negatively correlate with fasting insulin in male and uric acid for both sexes but was not significant ($P>0.05$).

In female, not male, glucose level also positively correlated with C-reactive protein, plaminogen activator inhibitor-1, Von Willebrand factor, they remained significant after adjustment potential confounding factors including BMI. Specially, in female group, leptin significantly correlated with glucose, after adjustment this relationship became gradually stronger (coefficient increased from 0.18 to 0.82).

Table 4.15 Correlation analysis between FPG and other variables in selected participants

Variable	Male			Female		
	Simple	Model 1	Model 2	Simple	Model 1	Model 2
BMI	0.071**	0.077**	—	0.096***	0.070**	—
WC	0.086***	0.082**	0.034	0.122***	0.076**	0.034
TG	0.234***	0.235***	0.223***	0.250***	0.226***	0.220***
HDLC	0.064**	0.027	0.055	0.112***	0.085***	0.103***
SBP	0.066**	0.025	0.003	0.102***	0.025	0.000
DBP	0.049*	0.046	0.021	0.004	-0.019	-0.043
Fructosamin	0.261***	0.267***	0.262***	0.470***	0.477***	0.479***
Uric acid	-0.066	-0.066	-0.080	-0.017	-0.004	-0.005
Log CRP	0.032	0.034	0.031	0.109***	0.088**	0.086***
Leptin	0.001	0.028	-0.065	0.182*	0.249**	0.283***
Insulin	-0.067	-0.028	-0.045	0.091	0.094	0.094
HOMA-IR	0.478***	0.511***	0.499***	0.749***	0.745***	0.758***
PAI-1	0.169	0.125	0.099	0.216***	0.224**	0.224**
TPA	0.008	-0.038	-0.041	0.060	0.052	0.059
TNF-α	0.050	0.108	0.094	-0.041	-0.064	-0.070
Fibrinogen	0.102	0.079	0.071	-0.078	-0.097	-0.095
IL-6	0.390***	0.410***	0.425***	0.527***	0.513***	0.515***
FFA	0.096	0.073	0.063	-0.093	-0.115	-0.119
Endothelin-1	0.106	0.144	0.128	-0.144	-0.166*	-0.168*
VWF	0.181	0.160	0.158	0.260***	0.213**	0.213**
FDP	0.037	0.010	0.007	0.042	0.018	0.016
D-dimer	0.033	0.040	0.031	0.131	0.129	0.125

In multiple correlation analyses, values in model 1 were adjusted for age, area, education, family history of diabetes, smoking, drinking and sedentary lifestyle. Model 2 further adjusted for BMI.
* P<0.05, ** P<0.01, *** P<0.001 for coefficient. In order to use the data information at the largest degree, the number of observations was different when analyzing on MetS components and other parameters, n=3910 for analysis on BMI, WC, TG, HDLC, SBP and DBP; n=914 for fructosamin and uric acid; n=2323 for Log CRP; n=269 for all other parameters.

4.6.2 Further analysis on fructosamin and HOMA-IR

Fructosamin and HOMA-IR were selected for further analysis. Table 4.16 showed adjusted odds ratios from multivariate logistic regression. After controlled possible confounders, both parameters were associated with increased risk of developing diabetes.

Table 4.16 Associations between diabetes and fructosamin, HOMA-IR

	Odds ratio*	95% CI	P
Fructosamin (n=906)	1.37	1.24-1.51	<0.001
HOMA-IR (n=266)	1.29	1.15-1.45	<0.001

* Odds ratios were adjusted for age, sex, BMI, area, education, family history of diabetes, smoking, drinking, and sedentary lifestyle.

5. DISCUSSION

5.1 Discussion of main findings

5.1.1 Prevalence of diabetes

In general, 7.7% and 21.0% of adults aged 35-74 years were observed with diabetes and IFG in Jiangsu province in the present study, which was much higher than any of the previous large-scale diabetes studies in China(17-19). In the study named InterASIA(19), conducted in 2000-2001 including a large representative sample of Chinese adult population with the totally same age span, the prevalence of diabetes and IFG were 5.5% and 7.3%, respectively. Our study was conducted in the year of 2002 around, however, it indicated a much higher rate compared to InterASIA study. The prevalence of diabetes in all of the groups was higher than that in InterASIA. Especially, marked increase in the proportion of people with IFG was found, which have been identified as risk factor for overt diabetes and cardiovascular disease(82), although there were two possible explanations for the difference. Firstly, diagnostic criteria for IFG used in our study were lower than InterASIA (5.6–6.9 mmol/l vs. 6.1–6.9 mmol/l). Secondly, as demonstrated above, Jiangsu province is one of the most developed areas in China. Its higher rate of diabetes than nationwide studies also possibly due to different population sampling results.

The latest large-scale study in China was the 2002 China National Nutrition and Health Survey (NNAHS), which had national representative sample from 31 provinces, autonomous regions, and municipalities. The prevalence of diabetes was 2.6% in Chinese adults aged 18 and over, but it reached into 4.3% and 6.8% in people aged ≥45 years and ≥60 years, respectively. And also, the prevalence of IFG was 1.9% in Chinese adults aged 18 and over, it increased into 3.4% and 4.9% in people aged ≥45 years and ≥60 years, respectively. The prevalence of diabetes and IFG increased with age, with higher increasing speed found in large city(103). Our study was conducted almost at the same time with NNAHS, but the corresponding results in the population with same age in our study were higher than this report. Except IFG criteria used in our study were lower (5.6–6.9 mmol/l vs. 6.1–6.9 mmol/l) which could explain part of difference in the IFG rate,

however, it still indicated the situation of diabetes and IFG was more serious than the average level of the country.

In contrast, estimated prevalence of diabetes in our sample is lower than that in some developed countries during the same period(13, 104, 105). For example, the US National Health and Nutrition Examination Surveys of 1999–2002(13) showed the adjusted prevalence of diabetes was 9.8%, using the same diagnostic criteria with our study. Results from the Diabetes Heart and Health Survey (DHAH)(105) carried out in Auckland, New Zealand in 2002-2003 reported the adjusted prevalence of diabetes was 9.3% all together.

The prevalence of diabetes increased with age and BMI status of both sexes in the present study, which was supported by many other studies throughout the world(13, 18, 19). And also, in accordance with the findings by Pan et al (18), it was higher in female and in better income family, which was also similar with other studies.

Our study has public health significance. It indicated that a large number of adults in Jiangsu province have diabetes or impaired fasting glucose because of large total population. Prevention and treatment of diabetes and its various complications, and reduction of risks of other chronic diseases should be urgently put on the agenda.

5.1.2 Prevalence of metabolic syndrome

The findings in our survey estimated that 12.3%, 21.8% and 30.5% adults aged 35-74 years living in Jiangsu were affected with metabolic syndrome applying to WHO, IDF and modified ATP III criteria. It can be easily found that the rate is increasing remarkably when comparing it with the results from the study in 1992, which indicated the prevalence of the syndrome was 13.3% using their own criteria referred to WHO, ATP III definitions(45). The adjusted prevalence was even higher than the results from another study also conducted in Jiangsu province in 2006(48) using the same definition (IDF criteria used). It can be explained in two ways. First, the population sampled was

different. The proportion of south areas in our study was higher than that study. The second, the age of subjects in our study was older than that study (people in 35 years old as youngest compared to 20 years old). So, these two differences may have concealed the increasing trend of metabolic syndrome. Other than the overall prevalence, the same conclusions were still drawn that the prevalence was higher in female and the elderly.

The metabolic syndrome was more common in female than in male independent of definitions in the current study, which was supported by other studies in China(48, 49). It was inconsistent to the study in Japan(41) which showed a higher rate in female, this mainly due to the latter study used a larger waist circumference cut-off value for females (90 cm) than for males (85 cm) based on the Japanese diagnostic criteria.

An interesting finding is the opposite age trend between genders when IDF criteria was applied. In female, the prevalence of metabolic syndrome increased with age. But in male, the prevalence decreased with the age. This was possibly due to prevalence of MetS components like central obesity (waist circumference) and low HDLC decreased with age in male. Similar report on inverse association between MetS and age in men can not be found so far. However, one study from China reported age was negatively associated with obesity in middle-aged and elderly people(106). Such a negative association between MetS and age in men may be due to effect of androgen levels on adipose distribution and metabolism. And also, westernized lifestyle characterized by a combination of excessive energy intake and inadequate physical activity may have less effect on old men compared to youngsters. Old men are likely to prefer traditional Chinese food and exercise more frequently, while young men may possibly consume more westernized food and spend the majority of time staying in office and at home.

5.1.3 Overweight and obesity

It has been clear from a large number of epidemiological studies that overweight and obesity were important modifiable risk factors for various chronic diseases like cardiovascular disease and diabetes(8). In the present study, BMI status was further

confirmed as the strongest modifiable factor for the development of diabetes. And also, BMI status was also proved to be significant risk factors for metabolic syndrome independent of definitions.

Overweight and obesity has been increasing in most parts of the world for several decades, so has in China(107). The epidemics of diabetes and obesity have reached a crisis level(108). The prevalence of overweight and obesity increased by 40.7% and 97.2%, respectively, among adults in China from 1992 to 2002(107). In our study, the prevalence of overweight, obesity, and overweight together with obesity was 25.6%, 3.9% and 29.5% all together according to WHO classification(102). The prevalence is higher in women and in urban area. It was in line with other study conducted in 2000-2001 in China(109).

Result from our study indicated that weight gain was particular risk factors for hyperglycemia and metabolic syndrome among originally normal weight population. Therefore, control of body weight is of great importance to the prevention and treatment of related chronic diseases like diabetes, hypertension and metabolic syndrome. Excessive caloric intake from fast food, insufficient exercise, increased reliance on automobiles, popularization of television, and so on all result in weight gain(108). Therefore, prevention strategy should be clearly targeting on these issues.

5.1.4 Non-modifiable risk factors

Effects of age, gender and family history of diabetes on diabetes and metabolic syndrome were analyzed in our study. Age and family history of diabetes were significant risk factors for diabetes after adjusted for confounders while sex lost its significance after the adjustment. However, women had significantly higher prevalence of diabetes than men in our study. Likewise, these three factors were also risks for metabolic syndrome in our study.

Gender difference, trend with age, and association between family history of diabetes and chronic disease like diabetes were well established and repeatedly supported by a great deal of studies. But also, gender difference had impact on diabetes as risk of other diseases like coronary heart disease(110).

Although these risk factors cannot be changed, prevention and intervention measurements should be focused on this population with these characteristics. That is to say, women, old people and people with family history of diabetes should be the emphasis population of prevention and control. In addition, it will be more cost-effective to screen such persons before modifiable risk factors in these persons were designed to be changed.

5.1.5 Modifiable risk factors

Sedentary lifestyle was identified as risk factors for metabolic syndrome defined by IDF standard in our study sample (adjusted OR=1.37, $p<0.05$). As described above, physical inactivity has been found, in both cross-sectional and longitudinal studies, to be an independent predictor of Type 2 diabetes(54). Appropriate frequency and intensity of exercise undoubtedly should be recommended as a prevention and treatment for Type 2 diabetes, metabolic syndrome, and some other chronic diseases.

Dietary factors were not analyzed in the current study. However, in many intervention studies, dietary factors were elucidated to play an important role and dietary modification was cornerstone of prevention and management of Type 2 diabetes and metabolic syndrome(57, 58).

Smoking was identified as risk factors for metabolic syndrome defined by WHO and IDF criteria in men and it was also increase the risk of metabolic syndrome defined by IDF and modified ATP III criteria in women. Although alcohol drinking was not identified as significant risk factors in our study. However, these two factors especially smoking were also found associated with an increased risk of type 2 diabetes(111) and metabolic

syndrome(112, 113) in many studies. Consequently, smoking cessation and limitation of alcohol consumption should be implemented in public health practice all the time.

In addition, an interesting finding in our study was that habitual tea drinking was found as protective factor for metabolic syndrome defined by modified ATP III criteria in men. To our knowledge, no study has reported this association. In a Japanese study, the researchers didn't find the inverse association between green tea consumption and metabolic syndrome(114). However, accumulating evidence indicates that consumption of tea, especially green tea, has potential protective effect on the prevention of many diseases especially cancer(115). Consumption of green tea was also inversely associated with risk for diabetes, which was reported in Japan(116). In animal experiment, whole teas significantly reduced abdominal white adipose tissue both in female and male mice(117), while abdominal obesity is exactly one of the MetS components. However, its protective effect still needs to be further verified in follow-up studies before a recommendation is given.

5.1.6 Agreement and applicability of different definitions

Due to lake of uniform definition for MetS, a number of studies, most of them were cross-sectional ones, tried to compare and evaluate currently available definitions. The prevalence of MetS differed from each other when different criteria were used in same research population. Even 5-fold difference in the prevalence was found(118). And also, remarkable differences in the biochemical and clinical profile of positive subjects diagnosed by different criteria were observed(118). The highest overall agreement was observed between IDF and modified ATPIII definition which was similar in different studies(119-122), which was also in accordance with our study (κ=0.79, highest in three comparisons). Validity of the definitions were also discussed and suggestions for modification were given in Italian(123),Korean(124), Japanese(125) population. However, there were also no consistent opinions on the validity or applicability of various definitions. In few prospective studies, risk predictive ability by different definitions were also compared like in USA(71).

Other than the comparison, in some countries, researchers also set specific diagnostic criteria suitable for specific population in their countries. For instance, Chinese Diabetes Society (CDS) put forward a suggestion of MetS diagnostic criterion based on research results on the disease in Chinese population in 2004(126). A committee of Japanese specialists also established a diagnostic criterion of Japan-specific MetS in 2005(127).

5.1.7 Weight gain

Results from our study showed that WHO and IDF criteria of MetS neglected 80% cases of hyperglycemia in originally underweight person, while modified ATP III criteria can detect more similar number of cases in the population. From this perspective, it indicates that ATP III criterion is more powerful than the other two definitions in Chinese adults from our study.

Results from our study indicated 10-year weight gain was particularly risk factor for diabetes and metabolic syndrome among originally normal weight population ($p<0.001$). It was also risk factor in some other BMI group, but the results were not consistent. It is possibly caused by a small number of participants in those categories. Another possible reason is lean people was originally prone to be malnutrition and weight gain made them nearer to normal standard, while the majority of obese people had already suffered from the disease 10 years ago.

Study conducted in Japan(56) indicated weight gain increased the risk of Type 2 diabetes even in relatively lean people. Although the conclusion were not confirmed, avoidance of weight gain, weight loss in overweight and obese people is important to reduce the risk of the disease.

Another different issue needs to be aware is called “insulin-induced weight gain”, which was found in the treatment of diabetes with insulin(128, 129). Study from UK(130) showed those who received insulin treatment gained, on average, 5 kg from the start of

the study. The coping strategies include limiting dose by increasing insulin sensitivity through diet and exercise (first-line treatments), insulin replacement regimens, etc(128).

5.1.8 Inflammation factors

In the present study, fasting glucose level was found positively correlated with interleukin-6, in both sexes adjusted for a number of confounding factors. Interleukin-6 is a cytokine that has abroad range of humoral and cellular effects, and elevated plasma interleukin-6 was associated with type 2 diabetes(131), which supports our results. And also, glucose level positively correlated with leptin, C-reactive protein, plaminogen activator inhibitor-1, Von Willebrand factor in female subjects in our study.

As reported by many epidemiological studies, biomarkers of low-grade systemic inflammation like C-reactive protein, plaminogen activator inhibitor-1, fibrinogen, Von Willebrand factor, leptin and other various adipocytokines were evaluated to be associated with diabetes and metabolic syndrome. For instance, leptin concentration was strongly correlated wit percentage body fat(132). High leptin levels, probably reflecting leptin resistance, predict an increased risk of diabetes. However, a protective association between leptin and diabetes was found after adjusting for factors related to leptin resistance(133). C-reactive protein (CRP) was considered as an important predictor of type 2 diabetes(62).

5.2 Implications

In general, the present study has mainly three implications.

One, this study would contribute to secondary and tertiary prevention in the province. Some participants were diagnosed and could also be treated in an early stage. Subjects with positive results would attach more importance to the treatment and management of diseases, so would their family. And also, a high proportion and large number of people were found with or at risk of diabetes and metabolic syndrome in Jiangsu province, which require being paid more attention.

The second, some associated factors were identified in the present study, which could serve as basis of prevention. In conjunction with other literatures, active prevention campaign can be done in the whole population aiming at altering modifiable risk factors and with emphasis on population with non-modifiable risk factors. It can also enhance people's concern of prevention and control and decrease the possibility of disease occurrence. Moreover, associated factors identified in our study may be similar in other Chinese population such as people living in other parts of the country, or Chinese overseas immigrants. Therefore, similar intervention and prevention suggestions can be put forward with certain cautions.

The third, prevention approaches and suggestions were proposed in our study to address these problems. As illuminated in the beginning, prevention is the most cost-effective method to deal with these problems. And also, it is the only feasible approach to help reverse the negative trends in the incidence of diseases.

5.3 Methodological discussion

5.3.1 The strength of the study

In general, the main strength of the current study lies in the quality control of anthropometric and blood parameters.

Anthropometric parameters like height, weight, waist circumference were measured by well-trained investigator, which made them more reliable than self-reported results. And also, health investigators were asked to take measurement as accurate as possible, and the mean value of three measurements was used for analysis.

Blood samples were collected in 3 different tubes for each participant by experienced professionals. Aside from samples in EDTA tube, all samples in non-anticoagulant and fluoride tubes were centrifuged in local health service center within 3 hours to separate

plasma. All samples were then refrigerated and stored at -20 ℃ until laboratory assays could be done.

Blood specimen under cryopreservation were then packed and marked with type and code, attached with necessary explanation document. All of them were transported with cold chain to central laboratory in Provincial CDC.

Blood variables like FPG and lipid profile were measured by enzymology method using automatic biochemical analyzer. Clinical sensitivity and specificity for the selection of enzymology method were considered. Reference serum was used for internal quality control everyday.

On the other hand, large sample size made it possible that the calculation of prevalence estimates and risk factors analysis. As describes in methodology part, the final sample size in the survey was 3914, which was larger than any one of theoretical values according to either diabetes or metabolic syndrome and could meet the requirement of analysis.

In addition, most potential confounders like gender, age, family history, etc. were carefully controlled. For example, stratification controlled effectively between-stratum confounding, standardization and multivariate analyses such as logistic regression, partial correlation were used to control the confounding.

5.3.2 The limitations of the study

Some limitations should however be pointed out in the present study.

Cross-sectional nature This is the major limitation of our study, which limits causal inference between exposure and disease since data on temporal sequence is lacking, although a cross-sectional study will preferentially identify chronic diseases because people with chronic diseases are more likely to be “in disease state” at the time of

interview(134).

Selection bias Bias can be usefully defined as s systematic deviation from the truth, which has potential impact on the quality of data(134). Cluster sampling method was used in our study. It has disadvantage of lower accuracy due to higher sampling error. Although integrated with stratified sampling, the sample in our study may not be representative for the area. There are several reasons for this. Firstly, because the main task of the project is follow-up of participants instead of prevalence estimation, compliance of subjects was the emphasis of consideration, and this is the main reason. So, although the sampling method was designed ideally, there was some inconsistency in practice. As a result, the sample size in urban area is relatively small while large in rural areas. It possibly underestimated the prevalence of disease due to possibly higher rate in urban area. Secondly, only 4 communities/villages in study area can not represent the whole province because the socioeconomic disparities exist from place to place. Thirdly, there was also non-respondent bias and incomplete response in our study. It is possible that person with disease were more likely to response than those completely well. Maybe subjects with positive health behaviors were more likely to response(134).

As explained above, the findings in the present study may not be representative and caution should be taken into account if generalizing to the whole population of Jiangsu province, let alone China. There are huge disparities in different areas within the country. For example, there are 56 ethnic groups and different demographic characteristics between areas. However, it is still a valid sample to compare gender differences and to identify associated factors for diabetes and metabolic syndrome in Jiangsu province.

Information bias First, observer bias may exist in our study. For example, diet and exercise information collected in different time may be different. Second, subject bias may typically take the form of recall bias(134), which mostly happens in case-control study. But, in our cross-sectional study, it can also exist. For instance, information about body weight 10 years ago and disease history may deviate from the truth.

Questionnaire issue Compared to self-reported questionnaire, ideally, interviewer-administered questionnaire may have several advantages: (a) High response rate. (b) The completeness of the answers can be more assured by this approach. (c) The interviewer can give guidance and explanations to those complex questions. However, it also has some disadvantages: (a) The subjects have to confront the interview which could influence their answers. (b) Variability due to differences in the approach used by the interviewer and in the interpretation of any replies(134). In our study, the interviewer were trained and also given survey guideline to read to ensure presenting material in a similar manner. However, it is difficult to exclude the possibility of interaction between the subjects and the interviewer(134). (c) The subjects have no time to consider their answers and/or change them after an initial response(134). In addition, the questionnaire used in our study may be too long for the subjects to endure the whole process and for interviewer to check it carefully, which possibly distorted the real information. And also, their contact information such as name, address was recorded, which could make some sensitive questions like family income imprecise. There were still some missing values there. Lastly, the questionnaire used in the survey was not validated.

Finally, regarding the association between some variables, such as 10-year weight gain and the metabolic syndrome defined by WHO criteria in the participants who were underweight or obese 10 years ago, our results may reflect some problems of statistical power, due to the small number of participants in those categories.

5.4 Follow up and intervention suggestions

5.4.1 Follow-up study

Given exposure status when measured will refer to “current status” and this is measured prior to disease onset, the issues of temporality of disease/exposure, recall bias will not, in general, affect cohort study(134).

For example, from this cross-sectional data we didn't find association between alcohol drinking and the diseases. Maybe people had changed their lifestyle like quitting from alcohol drinking after suffering from the disease.

For this reason, prospective follow-up study is more powerful methodology to identify this kind of issues. Our project is on its way. It will try to find causal relationship between metabolic syndrome/components and diabetes. And also, it can validate the prognostic power of different definitions of metabolic syndrome. It is the basis for prevention and control to establish health strategies in population on the basis of recognition of the epidemiological characteristics and its dynamic changes, risk factors, and health effects, etc.

5.4.2 Diet and lifestyle modification

It is clear from our study results that the prevalence of diabetes and metabolic syndrome is very high compared to other previous studies in China and it is still increasing rapidly in Jiangsu province. It can be assumed that a large number of adults in Jiangsu province have diabetes, impaired fasting glucose and metabolic syndrome because of large total population. Therefore, interventions should be implemented in Jiangsu as soon as possible.

Cumulative evidence from the prospective studies consistently showed a reduced risk for diet and other lifestyle modification on the development of Type 2 diabetes (57, 82, 84, 86, 87). And also, they are regarded as the basis in the prevention and management of Type 2 diabetes and metabolic syndrome.

Change of dietary factors is one of the most important approaches. Chinese Food Guide (2007), proposed by Ministry of Health, is a guideline for healthy diet. For example, diversity of food, increase intake of vegetable and fruits, consumption of milk and soybean or its products everyday, less oil and salt, exercise everyday and so on.

Exercise is the second important approach to deal with the problem. An appropriate frequency, intensity and duration of exercise undoubtedly should be recommended as a prevention and treatment for Type 2 diabetes, metabolic syndrome, and some other chronic diseases.

Control of body weight is of great importance to the prevention and treatment of these chronic diseases. And also, appropriate weight can be surrogate of control effect.

Many studies, also supported by the present study, indicated women, old people and people with family history of diabetes are at more risk of disease. So, they should be given priority in the practice of prevention and control. In addition, it will be more cost-effective to screen such persons before modifiable risk factors in these persons were designed to be changed. However, another important population is children. Special role in future society and fact of at more adulthood risk of chronic diseases should make them of special concern.

Moreover, smoking cessation and limiting alcohol consumption should be implemented in public health practice all the time.

5.4.3 Primary, secondary and tertiary prevention

Regarding the prevention of diabetes and metabolic syndrome, it can be classified into three levels:

Primary prevention aims at modification of the risk factors such as unhealthy diet, sedentary lifestyle, overweight and obesity, and so on, in high risk populations to reduce the occurrence of pre-diabetes and MetS components. Secondary prevention aims to prevention the development from pre-diabetes and MetS components to overt diseases. Tertiary prevention involves standardized treatment and management of diseases, for example, control of blood glucose to prevent the complications and improve the life quality.

Extensive prevention and control of disease in the society actually is not a research issue any more, but needs the cooperation and effort of many systems including government, NGOs, media, and all the people.

Developing a health system where prevention is recognized as the most cost-effective intervention is key to the fight against chronic diseases(135). However, In China, nearly 70% of Government expenditures focus on curative services in hospital and urban areas (135). Therefore, the emphasis should move forward to prevention and the range should be extended to rural areas where the majority of people live in. Especially in Jiangsu province, one of the most developed areas in China, more investment can be made for health promotion of chronic diseases in society.

6. CONCLUSIONS

In conclusion, our results indicate a high prevalence of diabetes, impaired fasting glucose and metabolic syndrome among middle-aged and elderly adults in Jiangsu province, China. We also found some modifiable and non-modifiable factors related to these diseases. Considering the tremendous economic and human resource costs, public health intervention programs and community-based strategies for lifestyle modification are of great necessity to address the problems.

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APPENDICES

Questionnaire on disease history and lifestyle

Investigation date： □□□□ year □□ month □□ day

Starting time of investigation： □□ hour □□ minute (24 hours system)

Area code: Suzhou=1 Changshu=2 Ganyu=3 Jintan=4 □

Name	_____ ID number □□□□□		
Family address	City town Street (Village) Building No House No		
ID card number	□□□|□□□□□□□□□□□□□□□□		
Contact information	Participant's office tel. □□□□-□□□□□□□□ Participant's home tel./mobile tel. □□□□-□□□□□□□□		
	Permanent contact tel.□□□□-□□□□ □□□□	Relationship with participant	

The information mainly comes from:	Participant=1 Dependent=2 Both=3 Others=4	□
Has venous blood been drawn for testing?	Yes=1 No=2	□
Has blood specimen been obtained after fasting?	Fasting＝1 Postprandial＝2 Not drawn=3	□

Investigator	_____ (Signature)
Investigation result	□ (Finished=1 Not finished=2 Rejected=3)
Quality controller	_____ (Signature)
Quality inspection result	□ (Qualified=1 Not qualified=2)

A. General Information

1. Name：

2. Sex： Male=1 Female=2 ☐

3. Date of birth：(yyyy/mm/dd) ☐☐☐☐/☐☐/☐☐

4. Time residing here (years): ☐☐

5. Occupation: Brainwork entirely=1 Brainwork mainly=2 Physical work=3 Physical work entirely=4☐

a. What main types of work have you done so far (in order) ①___ ②___ ③

6. Education: Illiterate=1 Primary school=2 Junior high school=3 Senior high school/technical secondary school=4 higher than junior college=5 ☐

7. Marital status: Single=1 Married=2 Divorced=3 Widowed=4 Separated =5 ☐

8. How many family members do you have (including yourself)? ☐☐

9. Average family annual income (RMB): ☐☐☐☐☐☐

10. How many people depend on this income? ☐☐

11. Percentage of monthly food consumption in monthly gross income in your home (%): ☐☐%

B. History of main diseases

B1.History of hypertension	Yes=1 No=2 Not certain＝9 ***(If your answer is "no" or "not certain", please go to section"B2")***	☐

a. Your age when first diagnosed: N/A=99 ☐☐

b. Rank of hospital making such a diagnosis: Province or higher=1 municipal (town)=2 county (district)=3 village=4 Not certain=9 N/A=8 ☐

c. Has health professional ever told you the type of hypertension? ☐

Essential＝1 Secondary＝2 Not certain＝9 N/A=8

d. So far, the highest level of blood pressure since first diagnosis (SBP/DBP mmHg): ☐☐☐/☐☐☐

e. Usual blood pressure (SBP/DBP mmHg): ☐☐☐/☐☐☐

f. Drugs you are taking for high blood pressure: Never＝1 Sometimes＝2 Often＝3 Regular＝4 ***(If your answer is "never", please go to section"B2")*** □

If yes, how long (months)? □□□

g. Have you taken antihypertensive in past two weeks? (Yes＝1 No＝2) □

If yes, drugs name 1._____ 2.

B2.History of diabetes	Yes=1 No=2 Not certain＝9 ***(If your answer is "no" or "not certain", please go to section"B3")***	□

a. How old were you when your diabetes was first diagnosed? □□

b. Rank of hospital making such a diagnosis: Province or higher=1 municipal (town)=2 county (district)=3 village=4 Not certain=9 □

c. Fasting blood sugar at that time: □□.□□mmol/l or □□□.□ mg/dl

d. Primary method you are using for glucose control: Dietary control＝1 drugs＝2 Nothing＝3 □

e. Are you using insulin now? Yes＝1 No＝2 Not certain=9 □

If yes, how long (months)? □□□

f. Are you taking oral hypoglycemic agents? Yes＝1 No＝2 □

If yes, how long (months)? □□□

g. Answered by women only ***(if you are a man, please go to "h"):***

Has health professional ever told you that you were suffering from diabetes when you were pregnant? **Yes＝1 No＝2** □

Has health professional ever told you that you were suffering from diabetes when you are not pregnant? **Yes＝1 No＝2** □

h. Has health professional ever told you that you were suffering from diabetic ophthalmic disease? Yes＝1 No＝2 □

i. Has health professional ever told you that you were suffering from diabetic nephritis? Yes＝1 No＝2 □

B3. History of hyperlipidemia (cholesterol) Yes=1 No=2 Not certain＝9 ***(If your answer is "no" or "not certain", please go to section"B4")*** ☐

a. Your age when first diagnosed: ☐☐

b. Rank of hospital making such a diagnosis: Province or higher=1 municipal (town)=2 county (district)=3 village=4 Not certain=9 ☐

c. Serum total cholesterol level at that time: ☐☐☐mg/dl or ☐☐.☐mmol/l

d. Are you controlling diet or adjusting dietary structure for decreasing blood lipid level at present? Yes＝1 No＝2 ☐

e. Did you take antihyperlipidemic drugs within last 2 weeks? (Yes＝1 No＝2) ☐

If yes, please specify the names 1. 2.

B4. History of obesity

a. Your weight at present (Kg): ☐☐☐.☐ Kg

① Your weight when you were young (25 years old) (Kg): ☐☐☐.☐ Kg

② Your weight ten years ago (Kg): ☐☐☐.☐ Kg

b. How old were you when you started becoming obese? ***(If your answer is "no", please print "00", and then go to "C")*** ☐☐

① How many kilograms did you increase in body weight in that year? ☐☐

② The most leading cause responsible for your weight increase do you think is: ☐

Diet increase＝1 Exercise decrease＝2 Illness＝3 Drugs＝4 parents obesity＝5 other=6 (Please specify)_____ Not certain＝9

③ Have you ever tried to reduce your weight? ***(If your answer is "no", please go to "C")*** Yes＝1 No＝2 ☐

Main methods you used for weight loss: ☐, ☐, ☐

Drug＝1 Dietary control＝2 Exercise increase＝3 surgery＝4
Chinese medicine＝5 Others=6 (Please specify)_____

Are you taking any kind of anti-obesity drug at present? (Yes＝1 No＝2) ☐

If yes, please specify the names 1._____ 2.

C. History of other diseases

(Rank of hospital making such a diagnosis: Province or higher=1 municipal (town)=2 county (district)=3 village=4 Not certain=9)

Name of disease	Suffering from this disease (Yes=1 No=2 Not certain=9)	Your age when first diagnosed or attacked	Rank of hospital making such a diagnosis
1. Coronary heart disease	☐	☐☐	☐
a. Myocardial infarction	☐	☐☐	☐
b. Angina	☐	☐☐	☐
c. Heart failure	☐	☐☐	☐
2. Brain stroke	☐	☐☐	☐

Type: ☐

1= Subarachnoid Hemorrhage 2= Intracerebral Hemorrhage 3= Thrombotic strokes 4= Embolic strokes 5= Uncertain type

Name of disease	Suffering from this disease (Yes=1 No=2 Not certain=9)	Your age when first diagnosed or attacked	Rank of hospital making such a diagnosis
3. Chronic renal disease	☐	☐☐	☐
4. Chronic gastrointestinal diseases	☐	☐☐	☐
5.Thyroidism disease	☐	☐☐	☐
6.Cancer	☐	☐☐	☐
7. Polycystic ovary syndrome	☐	☐☐	☐
8. Premature coronary heart disease (before 60 years old)	☐	☐☐	☐
9.Other diseases ( )	☐	☐☐	☐

D. Family history of disease

kinship	Total number	of hypertension	of diabetes	of obesity	of hyperlipidemia
Father		☐	☐	☐	☐
Mother		☐	☐	☐	☐
Brother	☐☐	☐	☐	☐	☐
Sister	☐☐	☐	☐	☐	☐
Son	☐☐	☐	☐	☐	☐
Daughter	☐☐	☐	☐	☐	☐

E. Smoking

1. Have you smoked at least 100 cigarettes up to now? (approximately 5 packs) ☐
Yes=1 No=2 Stopped=3 ***(If your answer is "no", please go to question No.7)***

2.Your age when starting regularly smoking (in full years of life)? **(at least 1 cigarette everyday, lasting at least half of year)** ☐☐

3. How many cigarettes do you smoke in a day? ☐☐

4. How many years have you being smoking regularly? ☐☐

5. Have you ever tried to stop smoking? Yes=1 No=2 ☐
If yes, How old were you when you started to stop smoking (in full years of life)? ☐☐

6. Have you ever used other types of tobacco? Never=1 Dried tobacco=2 Rolling cigarette=3 Snuff and chewing tobacco=4 ☐☐

7. How many persons smoke at home besides you? None=00 Not certain=99 ☐☐person(s)

8. How many cigarettes do they smoke in a day on average? Not certain=999 ☐☐☐Cigarette(s)

9. For how many hours are you surrounded by smokers so near that you can feel that smell during work? ***(if you are unemployed, please select "not applicable")*** ☐☐hours
None=00 Not applicable=88 Not certain=99

F. Alcohol drinking

1. Do you ever drink alcohol? **(Drinking alcohol twice or more a week, and 1 "liang" (50g) or more distilled spirits or equivalent)** ☐
Yes=1 No=2 Stopped=3 ***(If your answer is "no", please go to section "G")***

2. What age were you when you regularly drink alcohol (in full years of life)? ***(At least twice a week, and at least 1 "liang" (50g) distilled spirits)*** ☐☐

3. In the past 12 months, how much different alcohols listed below did you drink? **(None=00 Not certain=99)**

a. Beer 1bottle of beer=640ml 1can of beer=355ml	☐☐ Months per year ☐☐ Times per month ☐ bottles per time
b. Spirits 1"liang"=50ml	☐☐ Months per year ☐☐ Times per month ☐☐ "liang" per time
c.Wine 1"liang"=50ml	☐☐ Months per year ☐☐ Times per month ☐☐ "liang" per time
d. Rice wine or yellow wine 1"liang"=50ml	☐☐ Months per year ☐☐ Times per month ☐☐ "liang" per time

4. Have you ever tried to stop drinking? Yes=1 No=2 ☐

If yes, How old were you (in full years of life) did you start doing this? ☐☐

G. Living habits and physical activity

1. Average time for exercise in a week (hours)? ☐☐.☐hours

(If you never exercise, please print"00.0", and then go to question No.3)

2. How intensive?
Strong=1 (Running with weights or running fast, climbing, cycling fast, solo tennis)
Moderate=2 (jogging, field cycling, mild swimming)
Weak=3 (Walking, Swimming slowly, cycling(static), stretching) ☐

3.	Statistics of average time for activity	Weekday (hours)	Weekend (hours)
	Heavy activity (Running with weights or running fast, climbing, cycling fast, solo tennis, farming work, etc)	☐☐	☐☐
	Moderate activity (jogging, floriculture, field cycling, mild swimming, tennis, carpentry, etc)	☐☐	☐☐
	Light activity (Walking, Swimming slowly, cycling(static), stretching, etc)	☐☐	☐☐
	Very low activity (Sitting, Watching TV, Dining, etc)	☐☐	☐☐
	Nothing (Sleeping, lying, etc)	☐☐	☐☐
		Total: 24 hours	

4. Compared to the past 12 months, how is your level of physical activity in the last month?
1=More 2= Almost 3=Less 9=Unknown ☐

5. Compared to the majority of others in the same sex and age, how is your level of physical activity?
1=More 2= Almost 3=Less 9=Unknown ☐

6. Compared to yourself ten years ago, how is your level of physical activity? 1=More 2= Almost 3=Less 9=Unknown ☐

H. Diet

Now I am asking you some questions about food intake, particularly the frequency of food you usually eat. You are supposed to compare the issues in the last year and ten years ago when answering these questions. Please tell me the information of food/beverages you eat/drink daily, weekly or monthly.

	Food item	Average amount per time	≤1 time per month	2-3 times per month	1-2 times per week	3-6 times per week	≥7 times per week	Now	Ten years ago
1	Pork, beef, mutton (Liang)	□.□	1	2	3	4	5	□	□
2	Chicken (Liang)	□□.□	1	2	3	4	5	□	□
3	Freshwater fish (Liang)	□□.□	1	2	3	4	5	□	□
4	Seafood (Liang)	□□.□	1	2	3	4	5	□	□
5	Egg (stick)	□□	1	2	3	4	5	□	□
6	Milk (cup)	□	1	2	3	4	5	□	□
7	Green vegetables (Liang)	□□.□	1	2	3	4	5	□	□
8	Other vegetables (Liang)	□□.□	1	2	3	4	5	□	□
9	Fresh fruits (Liang)	□□.□	1	2	3	4	5	□	□
10	Pickle (gram)	□□.□	1	2	3	4	5	□	□
11	Fried Food (Liang)	□□.□	1	2	3	4	5	□	□
12	Legume (Liang) (soy milk, Tofu, etc)	□□.□	1	2	3	4	5	□	□
13	Green tea (Liang)	□□.□	1	2	3	4	5	□	□
14	Black tea (Liang)	□□.□	1	2	3	4	5	□	□
15	Flower tea (Liang)	□□.□	1	2	3	4	5	□	□

I. postscript by investigator

1. General estimation on the answers of this investigation. □

1=believable 2=Almost believable 3= Believable in some degree 4=Not believable

2. The ending time of investigation: □□ hours □□ minutes (24 hours system)

Registration Form for Body Examination

ID number□□□□□

1.	Have you taken antihypertensive today? Yes=1 No=2	□
2.	During the past 30 minutes, have you smoked, drank alcohol, drank caffeinated beverage, ate anything, exercised intensively? Yes=1 No=2	□
*[If the answer to the second question is "yes", rest **for 30 minutes** before measuring blood pressure.]*		
3.	Preparation for blood pressure measurement	
	a. Time record	□□ hours□□ minutes (24 hours system)
	b. Room temperature	□□℃
Sitting quietly for 5 minutes		
	c. Pulse in 30 seconds	□□times in 30 seconds
4.	First blood pressure after 30 seconds	SBP/DBP □□□/□□□mmHg
5.	Second blood pressure after 30 seconds	SBP/DBP □□□/□□□mmHg
6.	Third blood pressure after 30 seconds	SBP/DBP □□□/□□□mmHg
7.	Standing height (precision in 0.1 cm)	First measurement: □□□.□cm Second measurement: □□□.□cm
8.	Weight (precision in 0.5 kg)	First measurement: □□□.□kg Second measurement: □□□.□**kg**
9.	Waist circumference (precision in 0.1 cm)	First measurement: □□□.□cm Second measurement: □□□.□cm
10.	Hip circumference (precision in 0.1 cm)	First measurement: □□□.□cm Second measurement: □□□.□cm

Investigator's Signature:

Slip of medical examination results

ID number：□□□□□

Name Sex Age

Dear Sir or Madam,

Thank you very much for your participating in this investigation. What is listed below is your medical examination result in this research. We hope that it is helpful to you. Please do not hesitate to contact local Investigation Team if you find something wrong.

Measurement	Result of this investigation	Reference Value
Height	□□□.□cm	NA
Weight	□□□.□Kg	NA
Body Mass Index	□□.□Kg/m^2	<18.5 Underweight; 18.5-24.9 Normal; >=25 Overweight; >=30 Obesity
Waist Circumference	□□□.□cm	NA
Hip Circumference	□□□.□cm	NA
Waist to Hip Ratio	□.□□	Male: 0.85-0.9 Female: 0.75-0.8
Blood Pressure (SBP/DBP)	□□□/□□□mmHg	SBP <140mmHg DBP <90mmHg

May you healthy and happy!

Fieldwork Investigation Team, _____Center for Disease Prevention and Control

200_year_month_day

Enquiry about participation in the project "*Follow-up Study on Metabolic Syndrome and Diabetes in Jiangsu province, China*"

This study is a cooperative project between
Faculty of Medicine, University of Oslo
Jiangsu Provincial Centers for Disease Prevention and Control

Dear resident,

During the past 20 years, more and more Chinese people were suffering from chronic noncommunicable disease such as diabetes and metabolic syndrome (hypertension, hyperglycemia, overweight/obesity, etc). It has been one of main public health problems in China. Furthermore, it is especially serious in Jiangsu province due to its relatively developed economics, sustaining increase of aging people, and other potential factors.

This is to invite you to participate in a health research, which could help reduce and control the occurrence of such diseases and improve the health care quality in our city (town). You were selected randomly as a possible participant in this study because our research object is adults (both males and females) aged 35~74 years living in our province. The aims of this project are to evaluate the prevalence and incidence of metabolic syndrome and to describe the association between metabolic syndrome and health outcomes in our province.

If you agree to participate in this research, we will ask you some questions including health status in the past, diet, and some other issues like lifestyles. And also, we invite you to provide a blood sample for health and biological variables test. Some important results such as blood biochemical indexes will be informed to you in time.

There are almost no foreseeable risks for attending this research. By filling in the questionnaire, all you need to do is taking about 30 minutes. In the phase of blood examination, possible side effects may include local swelling after drawing blood, slight congestion, dizziness, etc. However, we have been well prepared to protect you, and to minimize potential harm to the lowest degree.

All information collected for the study will be kept strictly confidential, and will be only used for research purposes. Anyone unrelated to this study has no access to this information. All of your information will have your name and address removed so that you cannot be recognized from it when this study is finished. Neither your name nor information which could identify you or any of your will never appears in any research reports. Moreover, your participation is completely voluntary. You may choose not to participate, or withdraw from it at any time without giving any reason, without your medical care or legal rights being affected. Maybe you cannot receive too much direct benefits from taking part in this research, but it will have a favorable impact on public health in the future. Your participation will contribute greatly to our research. We thank you in advance for agreeing to help us out. If you have any questions or concerns about this study, please contact local or Provincial Center for Disease Prevention and Control.

CONSENT FORM

I have received the information about this study. I (or as legally representative of my dependent on the basis that she/he has received the above information and also wishes to participate in this study) hereby consent to participating in it.

Participant's (or dependent's) Signature: _____

Date: _____